(*Nothnagel's Encyclopedia of Practical Medicine*)

VARIOLA, VACCINATION
VARICELLA
CHOLERA, ERYSIPELAS
WHOOPING COUGH, HAY FEVER

BY

H. IMMERMANN, TH. VON JURGENSEN

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EDITED, WITH ADDITIONS

BY

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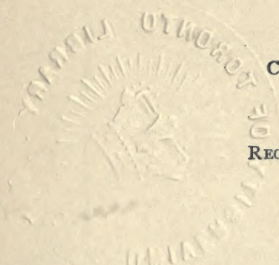Professor of Clinical Medicine in the University of Pennsylvania

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PREFACE.

THE excellence of the series of monographs issued under the editorship of Professor Nothnagel has been recognized by all who are sufficiently familiar with German to read these works, and the series has found a not inconsiderable proportion of its distribution in this and other English-speaking countries. I have so often heard regret expressed by those whose lack of familiarity with German kept these works beyond their reach, that I was glad of the opportunity to assist in the bringing out of an English edition. It was especially gratifying to find that the prominent specialists who were invited to co-operate by editing separate volumes were as interested as myself in the matter of publication of an English edition. These editors have been requested to make such additions to the original articles as seem necessary to them to bring the articles fully up to date and at the same time to adapt them thoroughly to the American or English reader. The names of the editors alone suffice to assure the profession that in the additions there will be preserved the same high standard of excellence that has been so conspicuous a feature in the original German articles.

In all cases the German author has been consulted with regard to the publication of this edition of his work, and has given specific consent. In one case only it was unfortunately necessary to substitute for the translation of the German article an entirely new one by an American author, on account of a previous arrangement of the German author to issue a translation of his article separately from this series. With this exception the Nothnagel series will be presented intact.

ALFRED STENGEL.

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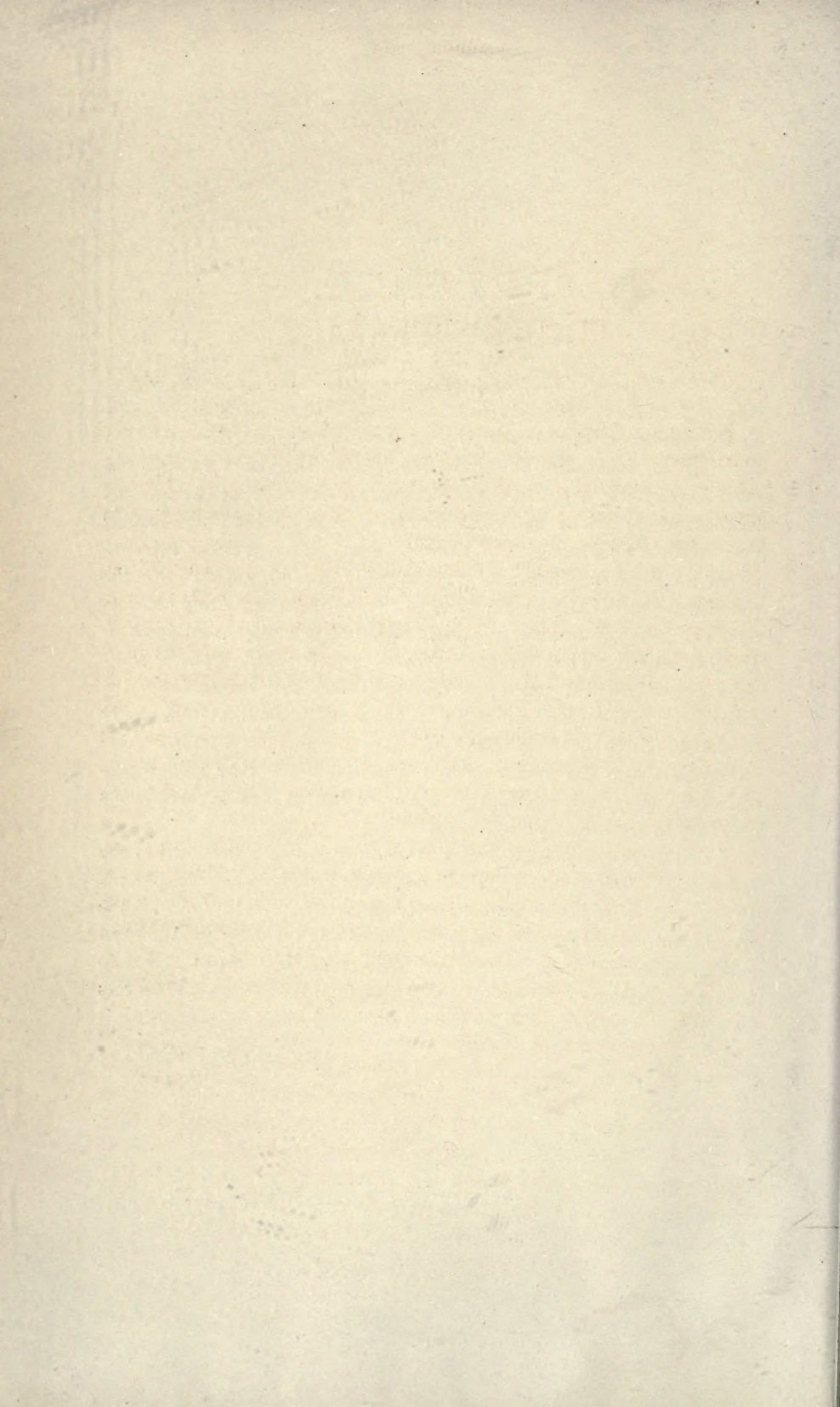
EDITOR'S PREFACE.

WHEN a courteous request came from the editor-in-chief of this great work that I should undertake the editorship of the second volume, I accepted Dr. Alfred Stengel's invitation—with alacrity, indeed, but at the same time with some misgivings as to my own fitness for the task intrusted to me.

As the work proceeded, I found that the literary excellence of the German text, and the detailed and comprehensive manner in which the respective authors had dealt with the several subjects upon which they wrote, left comparatively little to be done in the way of editorial comment or addition. Notwithstanding, I have not hesitated to interpolate sentences or paragraphs which were apparently required to explain or correct statements in the text. I have also embodied certain personal experiences gained in my own practice, extending over three and thirty years. These interpolations and additions are distinguished by being inclosed within square brackets.

The articles included in this volume treat of a number of diseases which are second to none others in importance, whether regarded from the standpoint of Preventive Medicine or as the cause of wide-spread sickness and death among the peoples which are unfortunate enough to fall under their ban. These diseases belong without exception to the class which the Germans so aptly name "Infectionskrankheiten" (infective diseases).

Dr. H. Lenhartz, of Hamburg, describes Erysipelas with much detail, and also gives an account of "Erysipeloid," a peculiar wound-infection to which Fr. J. Rosenbach gave the name of "Zoonotic Finger Erysipeloid." Dr. C. Liebermeister, of Tübingen, gives a very able historic, clinical, and pathologic description of Cholera Asiatica and of Cholera Nostras. Dr. G. Sticker, of Giessen, discusses Whooping-cough in a masterly way, and writes on Hay-fever under the name of "Bostock's Summer Catarrh"—a fact which reminds us that we owe the first classic account of this malady to Dr. John

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Bostock, of London, who read a paper upon it before the Royal Medical and Chirurgical Society in 1819, basing his description on his experience of the affection in his own person. Dr. Th. von Jürgensen, of Tübingen, writes with authority on Varicella; while Dr. H. Immermann, of Basle, contributes a monograph on Variola, including Vaccination, which has probably never been equaled for circumstance of detail and masterly argument. His vindication of vaccination as a preventive of smallpox is complete, unassailable, and conclusive.

As editor, I would wish to explain that I am not responsible for the "reformed" spelling adopted in this volume. It was necessary that the series of volumes of the Encyclopedia should be uniform in this respect, and accordingly I cheerfully acceded to the publishers' wishes in the matter.

In bringing my editorial labors to a close, I desire to record my grateful sense of the consideration and courtesy with which on all occasions I have been treated by my colleague, Dr. Alfred Stengel, and by the publishers of this edition of Nothnagel's "Encyclopedia of Practical Medicine." The work is a magnificent contribution to the literature of medicine. My earnest desire has been throughout that it should not suffer by the manner in which it has been done into English, or in which the translation has been edited.

JOHN WILLIAM MOORE.

40 FITZWILLIAM SQUARE, WEST DUBLIN.

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VARIOLA.

BY

H. IMMERMANN, M.D.

VARIOLA.

GENERAL CONSIDERATIONS. DEFINITION.

By Variola, Variolæ, or Blattern or Pocken (human as opposed to animal pox; true as opposed to false pox; windpox or varicella; English, smallpox; French, petite vérole) we understand a highly contagious and in severe cases very fatal acute disease, characterized by fever of a typical course, and by the appearance of a vesiculopustular eruption of the skin and the adjacent mucous membranes. The exanthem, which is in rare cases lacking (variola sine exanthemate), leaves behind in severe cases (variola vera) many permanent stigmata on the skin (pock scars); in lighter cases (varioloid or variolois) the eruption heals without leaving a scar. While, before the introduction of preventive inoculation or vaccination, the severe cases were prevalent in most epidemics, and while even now those who have not been vaccinated acquire a grave form of the disease, yet, where the disease occurs in the inoculated and revaccinated, it is generally in the milder form (the modified or mitigated variola).

In spite of the difference in severity, the two chief types of the disease, variola vera and varioloid, are not to be differently classified, but are of the same kind; for both types occur promiscuously in the same epidemic, arise interchangeably from each other, and are continually connected clinically by intervening transition stages. On the contrary, varicella (windpox) is an independent disease, differing from variola and varioloid and occurring in special epidemics; it is therefore not directly considered in this connection, but, as a special kind of disease, is considered in another part of this book.

LITERATURE.

The literature of variola is unlimited; even an approximately complete enumeration of all the works on smallpox of older and more recent times would easily fill the whole book. Therefore I quite give up the idea of presenting to the reader in this introduction to the consideration of smallpox such a review of the literature of the subject; in fact, in the preparation of the following list, only the results of a very

limited selection are collected and presented. On the other hand, in the course of the work it became necessary at different places to add to the text special bibliographic references on special subjects (etiology, symptomatology, pathologic anatomy, etc.). This has therefore been done whenever it appeared necessary (see the references at the close of the several sections in the following). From the general literature on variola I name, as especially worthy of attention, the following works and authors:

Rhazes: "De variolis et morbillis" (Arab. et Latin). London, 1756.—Constantinus Africanus: "De morbis cognoscendis et curandis," L. VII, c. 8. Basil, 1536.—Sydenham: "Observationes medicæ circa morb. acutor. historiam et curationem." London, 1676; also: "Epistola de observationibus nuper circa curationem variol. confluent." (1682). Oper. Select., Edit. III. Ludg. Batav., 1700.—Morton: "Pyretologia." Amstelodam, 1699.—Werlhof: "Disquisit. de variolis et anthrace." Hannoveræ, 1735.—Mead: "De variolis et morbillis liber." London, 1747.—Huxham: Oper., T. II u. III, London, 1744.—Boissier de Sauvages: "Nosolog. methodus," T. I, Pag. 422 *ss*. Amstelodam., 1748.—Van Swieten: "Commentar. in Boerhavii Aphorism.," T. V, Pag. 1 *ss*. Lugd. Batav., 1772.—Fr. Hoffmann: "Oper. omnia physic. med.," T. I, c. 7. Genev., 1740.—Storch: "Abhandl. über die Blatternkrankheit." Eisenach, 1753.—Cotugno: "De sedibus variol. syntagma." 1771.—C. L. Hoffman: "Abhandl. über die Pocken." Münster und Hamm, 1770.—De Haen: "Abhandl. über die sicherste Heilung der natürlichen Pocken." Wien, 1775.—Borsieri: "Institut. med. practic." Mediolani, 1785, T. II, 184.—Peter Franck: "De curandis homin. morbus." (S. 327, *ss*.) Ticin, 1792.—Hufeland: "Beimerkungen über die natürlichen Pocken." Berlin, 1798.—Rosenstein: "Kinderkrankheiten," 3. aufl. (translated from the Swedish by Murray). Göttingen, 1798.—Sarcone: "Ueber die Kinderpocken" (translated by Lentin). 1792.—Monro: "Observations on the Different Kinds of Smallpox." Edinburgh, 1818.—Thomson: "An Account of the Varioloid Epidemy." Edinburgh, 1820.—Elsässer: "Beschreibung der Menschenpockenseuche, welche" u. s. w. Stuttgart, 1820.—Stieglitz: "Horn's Archiv," Bd. XI, S. 187 ff.—Heim: "Horn's Archiv," Bd. X and XIII.—Albers: "Ueber das Wesen der Blattern." Berlin, 1831.—Eichhorn: "Die acuten fieberhaften Exantheme." Berlin, 1831.—Mühry: "Hufeland's Journal," Bd. XXVIII, S. 1 ff., and Bd. XXX, S. 128 ff.—Robert: "Précis historique sur l'épidémie, qui règne à Marseille," etc. Marseille, 1828.—Rayer: "Traité des maladies de la peau." Paris, 1835.—Petzoldt: "Die Pockenkrankheite mit bes. Rucksicht auf path. Anatomie." Leipzig, 1836.—Heim: "Historisch-kritische Darstellung der Pockenseuche im Königreich Würtemberg." Stuttgart, 1838.—Fuchs: "Die Hautkrankheiten.," 1840.—Rilliet et Barthez: "Maladies des enfants," T. II, pag. 430 *ss*. Paris, 1843.—Gregory: "Vorlesungen über die Ausschlags-fieber" (German by Helfft). Leipzig, 1845.—Williams: "Elements of Medicine," I, 192. London, 1846.—Simon: "Hautkrankheiten," 2. aufl., S. 127 ff. 1851.—Chr. H. Eimer: "Die Blatternkrankheit in pathol. und sanitats-poliz. Hinsicht" u. s. w. Leipzig, 1853.—Quincke: "Charité-Annalen." Berlin, 1855.—Wunderlich: "Handb. der Pathol. u. Therapie," Bd. IV, 1854.—Hebra: "Virchow's Handb. der Pathol. und Therapie," Bd. III, 1, 2 Erlangen, 1860.—Marc d'Espine: "Archives générales de médecine." 1859. Juin–Juillet.—Trousseau: "Clinique médicale de l' Hôtel-Dieu," T. I.—Stricker: "Studien über Menschenblattern" u. s. w. Frankfurt am Main, 1861.—R. Leo: "Archiv d. Heilkunde," Bd. V, S. 481.ff.—Kussmaul: "Zwanzig Briefe über Menschenpocken, und Kuhpockenimpfung." Freiburg, 1870.—W. Bernoulli: "Bericht an d. t. Sanitäts Collegium von Basel-Stadt" u. s. w. Basil, 1871.—Fiedler: "Jahresbericht d. Gesellschaft für Natur und Heilkunde in Dresden." 1872.—A. Guttstadt: "Zeitschrift d. königl. preussichen statist. Bureau," 13. Jahrg. 1873.—E. Müller: "Vierteljahresschrift für gerichtliche Medicin und öffentliches Sanitätswesen," Bd. XVII, 1872.—L. Meyer: "Deutsche Klinik," 1870, No. 6–10.—von Pastau: "Statistischer

Bericht über das städt. Krankenhospital zu Allerheiligen in Breslau für das Jahr, 1871" u. s. w.   Breslau, 1873.—W. Petters: "Prager Vierteljahrsschrift," 1876, Bd. I und II.—Knecht: "Archiv für Dermatologie und Syphilis," Jahrg. IV, S. 159 ff. and S. 372 ff.—Scheby-Buch: "Ebenda," Jahrg. V, S. 201 ff.—Curschmann: "Handbuch der spec. Pathologie und Therapie," herausg. von v. Ziemssen, Bd. II, 2 (2. und 3. Aufl.).—Barthélmy: "Recherche sur la variole." Thèse de Paris, 1880.—Guttmann, P.: "Berliner klin. Wochenschr.," 1881, Nr. 18, 19.—McChesney: "New York Med. Record," 1883, Nos. 13-15.—Galvagni: "Rivista clinica," 1884, Dec.—Th. Lotz: "Correspondenzblatt für Schweizer Aerzte," 1885, S. 36 ff.; 1886, S. 585 ff.; and 1894, S. 617 ff., S. 666 ff., S. 763 ff., S. 789 ff.—L. Pfeiffer: "Handbuch der spec. Therapie," herausg. von Penzoldt und Stinztzing, Bd. I, S. 217 ff.   Jena, 1894.

HISTORY.

In historic importance variola ranks above all other epidemic diseases. None of them has pursued the human race with such persistence and malignity, none has exerted such a determined influence on the history of the nations. Even if, at the present day, and wherever the protective power of vaccination extends, the destructive influence of variola seems less in many respects than formerly, we cannot even now speak of an entire removal of the danger of smallpox. Of the miseries of smallpox in the earlier centuries, and of the horror which was attached to the name of this pestilence, he alone can gain a correct idea who reads attentively the reports of competent observers; likewise he can understand why the question of the origin and source of smallpox has so busily occupied the minds of physicans and historians for more than a thousand years.

In spite of this the historic problem of variola has been very imperfectly solved, and the positive results gained, when compared with the efforts put forth, are remarkably scanty. The following points may be especially mentioned : It appears certain that the disease is of extra-European origin, and that it first set foot upon the soil of our part of the earth at the beginning of the middle ages. But the adjoining countries of Asia and Africa, especially the shores of the Mediterranean Sea, seem, even at the time mentioned, to have remained free of the plague. For neither in the Egyptian records, nor in the books of the Old and New Testaments, nor, finally, in the authors of Greek and Roman antiquity, are found reports or descriptions which can be referred indubitably to variola. And even Galen, to whom ancient writers, especially Rhazes, and also later writers (as, for instance, Haeser and Wernher), have wished to ascribe a knowledge of the disease, has left us nothing in his writings which really applies to variola. The so-called " Antonine Pest," described by this author, from which, among others, the Emperor Marcus Aurelius suffered (190 A. D.), and which has been especially considered in this connection, was not, according to the description, a smallpox epidemic.

In Hindustan, on the other hand, variola seems to have been indigenous from very ancient times (Holwell). This is shown by the fact that the old Brahman mythology recognized a special divinity (Takurani)

for this disease, as well as by the fact that the method of inoculation of the human smallpox for immunization is of great antiquity among the Hindus, and was practised by their skilled priests and attended by all sorts of religious rites. Also China, long before the beginning of our history, repeatedly had extensive smallpox epidemics, and also practised inoculation. Variola, according to the ancient Chinese records which are found in the "Herzenstractate wider den Blattern" (Chinese: Teonta-Hinfa), is said to have first entered this land at the time of the rule of Tschehus—that is, in the twelfth century before the Christian era—and not since then to have permanently left the country.

Though the reign of variola in far Eastern Asia is a very old one, it is, on the other hand, neither clear nor certain how later it found its way farther westward, and whether the western regions of the old continent—namely Asia Minor, North Africa, and Europe—received it from the East. According to another account, which is certainly historic but not more reliable, smallpox is said to have been indigenous from very ancient times in the interior of Africa, among the black races of men, and to have spread later from the heart of the dark regions northward as well as eastward even to the Red Sea. If this version is correct, it becomes clear why the first noted smallpox epidemic at the beginning of the middle ages occurred before the gates of Mecca, where, in the second year of the so-called Elephantine War (572 or 558 A. D.), an army of Abyssinians besieging the city was decimated by the plague which suddenly attacked them, and were obliged to return speedily home (Reiske). Variola was, according to one report, carried to the Abyssinians by the birds "across the sea," meaning probably the Red Sea. Whether the Abyssinians had previously seen epidemics of smallpox and knew the disease is not stated.

From this time, however, variola remained in Arabia, and soon gained a firm foothold in the adjoining regions of Asia Minor and North Africa. For when Rhazes (about 900 A. D.) wrote his famous treatise on "Smallpox and Measles," he could speak of smallpox as a disease long since known to his countrymen and spreading far and wide in the territory of Islam. At the same time, in his writings, he quoted fragments from the pandects of the Syrian physician and priest Ahron, who lived in Alexandria about 620 A. D. From these fragments of Ahron's writings it is certain that this author also was familiar with variola, which disease must therefore have been endemic in Egypt at his time (the seventh century of the Christian era).

But Europe also made the acquaintance of the pestilence in the sixth century, and since then it has not permanently disappeared. For that

fatal epidemic which in the year 581 A. D. broke out in southern France and northern Italy, and among others claimed many victims in the families of the Merovingian Kings Chilperich and Guntram, was undoubtedly an epidemic of smallpox, and not of the bubonic plague. Gregory of Tours * significantly distinguishes this pestilence from the plague, the " Morbus inguinaris," as " Lues cum vesicis " (also " pustulæ " or " pustulæ "), by which its identity with smallpox is sufficiently established. How and whence the disease thus came to Southern Europe is entirely unknown. It is possible, and is made even probable by the report of Marius of Avenches,† that two years earlier a similar epidemic raged in the Frankish possessions. (Hoc anno—morbus validus cum profluxio ventris et variolis Italiam Galliamque valde afflixit.)

With the introduction of variola into Southern Europe, near the end of the sixth century, it naturally spread rapidly in all directions. This is not the place in which it is fitting to follow more particularly this extension, however interesting the story is to the investigator. The disease advanced with slow course or quick springs, as it still does, and its contagious character and the social and international characteristics of the time served to aid its progress. The crusades in particular, with their movements of great hordes of men between the West and East, served to make variola more general in the Orient and Occident during the middle ages ; and the epidemics of that time were characterized by their fearful destructiveness. Likewise, the bold voyages of the Normans in all directions to all points of the compass must often have carried the germs of this pernicious disease from Southern Europe to other lands. Thus, besides England, Denmark was early invaded, and from that country smallpox penetrated even to Iceland, the " ultima Thule " of the ancients, in 1241 A. D. From Iceland the disease soon reached the Norman colony on the west coast of Greenland, and by repeated attacks of the pestilence exterminated the colony, so that from the beginning of the fifteenth century Greenland was almost forgotten in Europe, and three hundred years later had to be discovered anew.

Variola seems to have extended to Germany considerably later ; still later to Sweden and Russia, as the first unequivocal historic traces of its epidemic occurrence on German soil appear in 1493, and on Swedish and Danish territory in the sixteenth century. Of course, it cannot be said that variola did not come to these lands earlier and was not then recognized.

Very little scientific investigation seems to have been bestowed on

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* *Historiæ Francorum*, L. VI, c. 14, and L. x, c. 1.

† *Marii episcopi Histor. Francorum Chronicon*, 622.

the disease in the middle ages; at least very little work on it has come down to us from that time. The treatise of Rhazes already mentioned is almost the only work which is worthy of mention, and on it later writers, even to Sydenham and Boerhaave, base their conclusions. Rhazes ascribes variola, "by which only one or two of all are spared," to a boiling up of the juices, a kind of fermentation, by which the human body tries to rid itself of the smallpox material which dwells in it congenitally, and accordingly ascribes to the disease, on account of its universality, an absolutely critical value for the human species. The symptomatology is not badly described; and of the therapeutic directions, the recommendation of vapor-baths in the initial period seems, according to our modern ideas, somewhat doubtful; but the abundant use of cooling drinks in the further course of the disease and the rubbing of the body with oil and salt are still worthy of attention. Besides Rhazes, we must mention, as dating from a somewhat later period of the middle ages (about the middle of the eleventh century), the Salernian physician and author Constantinus Africanus. For with him, and through the communications on smallpox which he has left, the name variola (or variolæ), which had already occurred in the chronicles of Marius of Avenches (see above), but which had been used promiscuously for different kinds of pustular and papular affections, first became the permanent Latin term for smallpox. Apart from this, the papers of Constantinus, who relies wholly on Rhazes and the Arabians, contain nothing original.

According to some, the word "variola" was formed as a diminutive from the Latin word "varus" (node); according to others, it originated from the Greek word "αἴολος" (variegated, spotted). The German names "Pocken" and "Blattern" are borrowed respectively from the Dutch "Pocke" (pocket, purse) and the German "Blatter" (blister), and refer to the form of the exanthem, as also does the English term "small-pox." The prefix "small," equal to "klein," which corresponds to the "petite" in the French term "petite-vérole," came into use for the first time later on, after the appearance of syphilis in Europe (1494), when the papular and pustular syphilides began to be called "grosse Blattern," "Grosses véroles," to distinguish them from variola.

With the discovery of America in more modern times, variola took another step toward establishing its position as a universal pestilence. In America the disease had not previously existed, but it was soon introduced by the Spanish conquerors. In 1527 it had already reached Mexico, the kingdom of the Aztecs conquered a short time before by Cortez, and within a few years it created fearful havoc among the inhabitants. Favored by new arrivals from Europe, and still more by

importation from Africa by means of the negro slave-trade, it gradually subdued the other American tribes, and did far more to bring about the progressive annihilation of the aborigines than the firearms and fire-water of the white man.

Smallpox reached the highest point of its distribution and intensity in Europe in the eighteenth century. No land in our part of the world was then for any length of time free from the pestilence, and with the gradual withdrawal of the bubonic plague smallpox became the dominant pandemic in the fullest sense of the word. The records of the mortality from smallpox at this time are fearful; in England, for instance, it accounted on an average for a tenth of the total mortality; in France, about 30,000 people died annually; in the regions then ruled by the Prussian monarchs, according to Junker's[*] reports, not less than 26,646 perished from this disease in the year 1796 alone. Children were attacked with special severity, but even among the most advanced in years, each new epidemic likewise demanded numerous victims. The disease spared neither high nor low, spread its terrors in the huts of the poor as well as in the dwellings of the rich, and even penetrated into the palaces of princes and more than once threatened with the danger of total extermination the representatives of European dynasties. And, finally, if the number of the dead was gradually becoming fearfully large, still greater after each new epidemic was the number of those who, escaping indeed with life, had to endure for the rest of their days all kinds of defects or at least disfigurements as a result of this frightful disease. No wonder was it, then, that, in the midst of such continuous smallpox misery, finally a wide-spread humor of despair found expression in the light words, " From smallpox and love but few escape."

The time was hard for physicians also; above all, they had the depressing sense of standing powerless before the prevalent disease. The scientific views about its nature had become somewhat clearer since Sydenham. They knew that variola was a specific disease, and no longer identified it with measles, with which, strange to say, it had been often confused in earlier times. The contagious nature of the disease and the usual modes of infection had become familiar ideas to physicians as well as to laymen, and had gradually led to certain pro-phylactic measures, especially isolation of the sick, fumigation of their belongings, etc. Likewise the treatment of smallpox was somewhat modified,—this also through the efforts of Sydenham, and afterward of Boerhaave,—so that in place of the intensely diaphoretic measures, a

Archiv für Aerzte und Seelsorger wider die Pockennoth. Halle, 1798.

more cooling treatment was used, with some advantage to the patients, who were tortured by heat. But all this really availed little in the face of the general calamity; for afterward, as before, the patients in small-pox times died in masses, so far as they were attacked with the graver forms of variola, which unfortunately was very often the case.

The first glimmer of hope that things might perhaps become brighter and better had penetrated from the East into Europe in the third decade of the eighteenth century. About this time (1721) the news of the method of inoculation practised in the Orient from ancient times came as glad tidings by way of Constantinople to England, and later to the Continent of Europe. It caused great excitement, and, I may add, justifiable surprise. The soil for the reception of this method of treatment had been already somewhat prepared in the occidental world of culture; as already in Europe, at least at certain times and in some regions, the custom of the so-called "smallpox purchase" (Pockenkaufen) had come into some use. They exposed an apparently healthy person for a brief time to the contagion of a mild case of smallpox, in the hope that he would have a light form of the disease, and thus become immune to infection with a grave form. The experiment, uncertain in regard to the control of the *contagium volatile*, repeatedly proved itself to be dangerous in respect to the results of the smallpox disease obtained by the "purchaser." The direct inoculation of the small-pox virus promised safer results; at the same time, a favorable rumor preceded the latter operation that, with suitable choice of inoculation material and with attention to other tested precautions, the inoculation variola was relatively free from danger. The guiding idea was the same. The operation had finally—slowly, of course, but indisputably and with compelling force, through experience, the mother of all wisdom—penetrated into Europe to the aid of humanity seeking rescue from the miseries of smallpox.

Experience—not a single or ephemeral one, but one which had been many million times repeated, and for more than a thousand years—had taught that smallpox, like love, naturally attacks nearly all men, but that, with rare exceptions, each one has smallpox once only in his life, and generally receives with the passing of the pestilence the inestimable gift of permanent immunity; and, further, that this favor is not proportioned to the severity of the attack, but is equally distributed to the mildest and severest cases. Here was given an important index for a real prophylaxis—a desideratum which consisted in nothing less than the acquisition of variola itself under the most favorable possible conditions. The simple purchase of smallpox had not fulfilled these con-

ditions. Cautious inoculation seemed to promise better things, and, in fact, its results were much better. However, it was proved to be by no means free enough from danger to be generally adopted as a prophylactic measure or to gain official sanction in the countries of Europe during the eighteenth century.

As the history of inoculation must be mentioned again later—under "Vaccination"—this brief notice may be sufficient here. It may be simply added that this remarkable episode in the history of smallpox as a matter of fact, so far as Europe is concerned, drew to a close with Jenner's publication about the end of the century in question.

Jenner's immortal service, the discovery of vaccination in place of inoculation with the virus of variola (or variolation), is the greatest sanitary fact of all times, and is not the less so because of the fact that in individual cases intentional vaccination had been practised before. Jenner's conviction that vaccination gave to the world a real, easily accomplished, and safe means of protection against the destroying angel of smallpox was founded on studies and observations continued for years; it was confirmed by the series of experiments undertaken by him, and was published, to the general advantage and profit, in his three consecutive works on the influence of vaccine (1798–1800). After the publication of his first work, in 1799, the practice of vaccination on a large scale was immediately begun, not only in England, but in almost all countries on the Continent, and the first public Vaccination Institutes were forthwith founded in London and Vienna. From that time, the history of variola has been inseparably connected with that of vaccination, so far as the influence of European civilization extended; for endemic occurrence, epidemic spread, and even individual susceptibility to human smallpox, during the nineteenth century and within the limits of civilization, have everywhere acquired a fixed relationship to the administration and achievements of protective vaccination. Outside of these limits, on the other hand, and, to speak more definitely, wherever the knowledge of vaccination has not penetrated, or where it has not found acceptance, the reign of variola is to-day very severe, partly from wretched surroundings, as in distant regions of Asia, Africa, and in non-civilized portions of America. Therefore the prevailing influence of vaccination on the form of variola in the nineteenth century cannot well be doubted; for this reason, it seems best to interrupt the historic consideration of variola at this point to resume it at a later time (in the consideration of "Vaccination").

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ETIOLOGY AND PATHOGENESIS.

GENERAL ETIOLOGIC FACTS.

THE history of variola teaches very conclusively that the disease is neither dependent on atmosphero-telluric influences nor is it bounded by climatic limits. Like all truly contagious diseases, of which variola may well serve as the prototype, the pestilence attaches itself to men, and the intercourse of men and geographic relations are concerned only in so far as they affect this intercourse. By this we mean that a central location, accessibility, and density of population have always favored the epidemic extension of the disease. But even the most remote regions, as history also teaches (Iceland and Greenland), may be attacked and severely visited, as soon as the disease is brought to them from anywhere, and even thinly populated districts may suffer from an epidemic, if only any communication is kept up, so as to make the transmission of the contagium possible.

Susceptibility to the disease plays a very important part. Besides the always necessary entrance of the specific agent of the disease, it constitutes the other factor which is necessary for the occurrence of the infection. Only where a sufficient individual susceptibility to variola exists can the contagium of smallpox act in isolated cases, and only when a sufficient number of susceptible individuals are in a community can a smallpox epidemic result from a single case.

Natural susceptibility to smallpox is very wide-spread, almost universal. Before the introduction of vaccination very few escaped from the disease, and now protective inoculation, if correctly applied, acts in nearly all men at least once in their lives, a fact which may be used indirectly as proof of the above statement. However, in earlier times there were certain individuals (among them the well-known names of Boerhaave and Morgagni) who, as is well known, though many times exposed to smallpox, never acquired the disease. Likewise it is now observed in very rare cases that in a few individuals vaccination not only does not succeed, but that all attempts at revaccination persistently fail. On what this natural and at times permanent immunity to variola and vaccination depends is not at all clear. A temporary immunity is, however, rather frequently observed, but its conditions are very unsatisfactorily explained. The fact is that in the prevaccination period, which

may be considered as the standard in this case, many people were exposed once or oftener to natural smallpox infection with impunity; nay, more, were even inoculated with smallpox with impunity, and yet some time later became susceptible, and were attacked by the disease. Similar observations have been repeatedly made more recently in those who have not been inoculated. These things can be explained only on the supposition of a temporary immunity. In those who have been vaccinated and revaccinated analogous evidence can be less strictly deduced, as the protective power of vaccination has no single, fixed duration. It seems undeniable that outside of the admissible limits of possible protection by inoculation (and therefore independently of it) conditions of temporary immunity exist which render the individual for the time being safe from infection. In so far as the question concerns, not those who are otherwise sick (see later), but the healthy, the phenomenon is entirely beyond our comprehension.

Apart from this, the natural susceptibility to variola belongs not only to the overwhelming majority of the human race, but without exception to all ages. The fetus in the mother's womb may be infected, but this generally happens only when the mother herself is attacked with variola during pregnancy. If a pregnant woman has smallpox, she usually bears children who either have, at birth, marks of the exanthem or are attacked with variola so soon after birth that, taking into consideration the usual time of incubation, an intra-uterine infection is the only possible explanation. In rare cases, however, a mother who was apparently free from the disease, during a smallpox epidemic, has borne children with the marks of the disease, although in some of the observations, the mother may have had a slight attack of variola, but so slight that the diagnosis was doubtful. [Curschmann considers that some of these infrequent cases may be explained on the hypothesis that the mother suffered from variola sine exanthemate, and so became the source of infection to her unborn child.]

The confined position of the embryo in the uterus offers a powerful protection, of course, against the entrance of the smallpox contagium from without, so long as the mother herself has not taken the disease; on the other hand, it is evident that so soon as this happens, the protection is withdrawn and the danger of transmission to the fetus, on account of its intimate relation to the maternal organism, is especially great. This logically explains the almost universal occurrence of intra-uterine infection when the mother has the disease, and the extreme rarity of the same when the mother is spared. Probably in both cases the placental circulation plays the rôle of infecting medium; but in case of the

disease in the mother, the influence of simple contact should also be thought of.

[From his experience, John MacCombie, formerly of the Southeastern Smallpox Hospital, London, considers that the liability of the fetus to smallpox is not great, but it appears to increase directly with its age. It is, however, exceptional to find that the children born of variolous mothers, even during convalescence, have had smallpox *in utero*, or that they are suffering from the disease at the time of birth. There is some reason to believe, indeed, that they are more or less protected against smallpox by the mother's attack. Of half a dozen infants born of variolous mothers which have come under MacCombie's observation, only one had smallpox at the time of birth. But infants have been born at the full time who had evidently passed through an attack of smallpox *in utero*. Rayer gives an illustration of smallpox in a fetus, and MacCombie states that cases have been recorded of infants showing the eruption of the disease well developed at birth, the mothers not having had smallpox. In one such case, he adds that the mother is said to have contracted smallpox from her infant. Sir Thomas Watson saw no reason for doubting that the unborn beings may pass safely through the disease while in the womb, and derive from that attack the customary immunity for the future. In support of this opinion he quotes his namesake, Sir William Watson, as describing in the *Philosophical Transactions* an instance in which the scars left by the pustules were visible upon an infant at its birth. This child was afterward inoculated without taking the disease. Its mother, who had previously had smallpox, when far advanced in pregnancy nursed a servant ill of smallpox, and so conveyed the disease to her unborn child. Sir Thomas Watson also mentions the following striking case. A woman was inoculated by Dr. Pearson with smallpox in her sixth month of uterogestation and had the disease severely. Her child was afterward twice inoculated with smallpox matter, but without effect. As to the channel through which the fetus becomes infected, Curschmann cites a remarkable instance which would go to prove that in such cases infection takes place rather by simple contact than through the mother's blood. A woman servant, aged 22, in the fifth month of her pregnancy, suffered from varioloid from November 20 to December 12, 1870. On December 28th fetal movements suddenly ceased. On the 31st a five- to six-months' child, evidently already some days dead, was born. It presented a well-formed smallpox rash in the stage of suppuration, covering the whole body—least marked on the face and most abundant on the back and buttocks. The appearances were such as to place the time of death (on

December 28th) somewhere between the sixth and eighth days of the disease. This would give an incubation of at least 10 to 14 days, on the assumption that infection took place toward the close of the mother's attack.]

The newborn children in the first months of life can be infected by their surroundings in the usual way, and, according to my experience, this happens very frequently if they come into contact with smallpox patients. I cannot at all subscribe to the view that the natural susceptibility to variola is very slight in these first months of life as compared to the condition during the following years of childhood; this idea is, in all probability, based on an inexact record of facts. It is true that the disease in very young children is rarer, inasmuch as, in neighborhoods free from smallpox, they less frequently have opportunity to be infected elsewhere; but it is not true that they are more immune than older children when they are actually exposed to the chance of infection. Protective vaccination is, therefore, not less necessary for them than for older children, whose susceptibility to variola is generally recognized.

The marked participation of children in the smallpox epidemics of the prevaccination period is a fact of great interest in the history of the disease. It should not be inferred from this, however, that the natural susceptibility to variola is greater at this age than in adults. The true reason is that the disease is so contagious, and extensive epidemics used to occur so frequently, that, in the absence of protective inoculation, a respectable majority of all the living were infected during childhood. Variola, therefore, acted in those times like measles, which is still generally recognized as an epidemic children's disease, because it is very contagious and very few escape its influence for a longer time than childhood.

As concerns variola, a complete change has been brought about in the nineteenth century, as, under the dominating influence of early vaccination in all countries, children are generally spared now on account of the prophylactic effect of the first inoculation. But the years of puberty and the next decade, and even up to the fortieth year, are subject to the most severe attacks, because, revaccination not being practised, the influence of the first vaccination is entirely exhausted. But other ages, even to extreme old age, as formerly, still regularly pay their tribute in so far as a previous attack of variola or a relatively frequently repeated vaccination has not destroyed the susceptibility. After all is said, there seems to be no definite influence of time of life on natural susceptibility, and all ages are apparently equally predisposed to smallpox.

Sex also plays no important part in predisposition to the disease ; men generally are infected as easily as women. It has been noticed, however, that in the latter, menstruation and pregnancy somewhat increase the susceptibility. It is also certain that smallpox is often extremely malignant in pregnant women. The fact that, in great epidemics of smallpox, the number of cases among men is often greater than among women is doubtless due to the fact that their social position brings men more frequently into contact with the disease.

The influence of race is perhaps of some importance. At least it has been shown that those belonging to the colored races (negroes and Indians) are subject to an especially grave form of the disease. Hence it appears that the natural susceptibility is even greater among these than among the white races.

The relation of variola to other diseases is interesting ; it varies with the nature of the latter. Chronic diseases have no influence on the susceptibility, and even the infectious chronic diseases—as, for instance, tuberculosis and syphilis—offer no protection against smallpox. The same is true of many acute, non-infectious diseases. A peculiar position is, on the other hand, occupied by certain acute infectious diseases, and especially by the acute exanthematous diseases (measles, scarlet fever) and by typhoid fever, as it is well known that during their continuance an infection with variola is very rarely added to the already existing infection. Perhaps a similar preventive relationship is afforded by influenza, whooping-cough, and malarial fever (Rosenstein). Measles, scarlet fever, and typhus during the convalescence period act quite differently after the decline of the fever. Then the variola contagion is easily acquired, if there is an exposure to infection and if the patient has not been otherwise rendered immune.

Positive experience teaches that double infection with measles, scarlet fever, and abdominal typhus [that is, typhoid or enteric fever] on the one hand, and smallpox on the other, may now and then occur (Steiner, Fleischmann, Simon). In what degree a similar preventive relationship exists between infectious diseases other than those named—as exanthemic typhus, relapsing fever, etc.—and variola is still to be ascertained. That variola infection often occurs in convalescents from typhoid fever has been frequently noted, as by Curschmann; I myself can assert the same from my own experience.

A permanent abolition of the natural susceptibility to variola is nearly always brought about by one attack of the disease, whether this attack is severe or mild. The knowledge of this fact is as old as the disease itself ; long before the beginning of our era, it was used in India and in China in the way of direct variolation as a prophylactic measure.

It is analogous to the permanent immunity acquired by one attack of certain other contagious diseases (measles, scarlet fever, etc.). There can scarcely be any doubt that the still unexplained mechanism which causes this immunity is really the same for variola as for the other contagious diseases.

However, cases of two or more attacks of variola in the same individual have occurred, although rarely, which show that permanent immunity cannot be promised with absolute certainty. The same thing may be observed in scarlet fever, and still more frequently in measles. Among these second attacks, we have to distinguish between relapses (or immediate recurrences of the disease) which are due not to a new infection from without, but to the residue of the original smallpox virus, and recurrences by renewed infection from without, when a longer time usually has elapsed between the first and the second attack.

The relapse is due to a not perfectly destroyed susceptibility to the disease, while the later recurrence is due to a predisposition which has with time been reawakened. Rarest of all, without doubt, are the true relapses, but such are really now and then observed. Somewhat more frequently, though still rarely enough, second attacks occur, between which and the first attack (experienced in youth) a series of decades usually intervenes. Whether second attacks are more to be expected when the first attack was quite mild, as has been asserted, has by no means been proved. Different examples, however, teach us that second attacks may also run a severe and even fatal course.

True relapses have been observed by Michel (in 2 cases) and by Hernick among recent writers. Louis XV, king of France, died at the age of 64 of confluent smallpox (May, 1774), although he had already had the disease in his youth, when he was 14 years old. F. v. Hebra gives a bad prognosis to the second attacks; probably this opinion is based on the fact that these second attacks usually occur in the very old, and that any acute infectious disease accompanied by fever is very deleterious in old age.

Vaccination affords the same protection as variolation ; but in most persons the former destroys the susceptibility for variola only for a time, and not permanently, as does the latter ; therefore revaccination can again destroy for a time the reawakened susceptibility. Finally, variola is much milder and less dangerous in those who have been vaccinated and revaccinated than in those not inoculated. This will be discussed more in detail in another place, under " Varioloid," and " Vaccination."

There has been no controversy about the nature of smallpox since the time of Sydenham and Boerhaave. Before their time, on the con-

trary, much was said of the possibility of an autochthonous origin of variola through atmospheric and telluric influences, sidereal constellations, etc., and also about the mode of transmission of the contagium. The specific and essentially contagious character of the disease has since then been decided. By this we mean that, according to all experience, the cause of variola is always the same ; that the smallpox virus is a unity, and also one peculiar to this disease alone ; that this virus is reproduced in the bodies of smallpox patients ; and, finally, that the disease arises only by immediate or mediate transmission of this virus to a susceptible individual.

The virulence of the smallpox agent is in all probability very variable, as is assumed for other disease poisons (scarlet fever virus, etc.). Besides the different degrees of individual susceptibility, this second factor has a marked influence on the severity of the prevailing smallpox cases. This influence of virulence was most clearly expressed in the prevaccination period, in which mild and grave smallpox epidemics were distinguishable, just as we may now distinguish mild and malignant epidemics of scarlet fever, measles, etc., the varying character of which can be explained only by the assumption of a temporary difference in virulence of the exciting principle. At present, in variola especially, the influence of virulence, while not entirely ignored, is kept more in the background ; the place in the foreground is now occupied by the idea of individual susceptibility. As this susceptibility has been very much weakened by the introduction of vaccination, and the severity of smallpox epidemics depends almost wholly on the number not vaccinated or not revaccinated in the population, the virulence is only secondary in importance.

The smallpox poison is no doubt contained in the smallpox exanthem. The positive results of inoculation prove this. The contents of the pocks are most virulent when they begin to be turbid ; that is, at the transition from the vesicular to the pustular stage. But the contents are quite virulent before as well as after this stage, and even the dried crusts, the cast-off scabs of the pock in convalescence, are still quite infectious, so that they were formerly used for inoculation, and sometimes with positive results. According to this, a smallpox convalescent is dangerous to the community so long as such remains of his disease are to be found on his body. (See Prophylaxis.)

The physiologic secretions and excretions of the smallpox patient (salivary, nasal, and bronchial secretions, and urine and feces) are, however, not virulent so long as they have not become infected from the eruption on the skin and mucous membranes by the pus or scabs. Inoc-

ulations with these secretions, with the above limitation, were made many times, in the days of inoculation, but always with negative results.

With regard to the blood, however, the views of the older writers are contradictory, which is perhaps due to the fact that in the later stages of the disease the blood loses its infectious character. In our time, inoculation experiments with variolous blood from man to man have not been made, for reasons which are easily understood ; Zuelzer, however, succeeded, by means of inoculation with fresh variolous blood, in producing in an ape typical variola with initial fever and an extensive smallpox eruption. L. Pfeiffer also asserts that by inoculation of the blood of a smallpox patient (in the initial stages of the disease), and also by the inoculation of blood from a variolous pock in the papular stage of the exanthem, local (vaccine-like) pustules can be produced in calves. From this it cannot be doubted that the blood of a variola patient in the early stages of the disease really possesses infectious properties and contains in itself the pathogenic contagium. (Compare later, under Parasitology.)

Of the greatest importance for the epidemic spread of the disease is the fact that the contagium existing in the pock-contents is volatile (*contagium volatile*). This signifies that the specific agent possesses the power, by means of effluvia from the patient, of mingling mechanically with the surrounding atmosphere and of infecting the air to a distance. This volatility is not only a property of the contagium of smallpox, but it is so to a very high degree, and on this peculiarity rests the great danger of infection. This danger is naturally greater where many patients are crowded together and where the eruption is extensive. For a susceptible person, the danger is greatest if he comes often to, or stays long in, a smallpox locality or in the neighborhood of a smallpox patient, while with increasing distance the "chance of acquisition" rapidly lessens. But the vitality of the volatile variola poison is so great that pathogenic transmission of it for great distances (100 meters and over) through the open air is by no means unheard of.

The volatile contagium of variola, according to all appearances, develops its infectious power mostly from the exanthem, as infections arise most frequently during the exanthematous stage of the disease (in the periods of appearance, development, and maturation of the pocks).

[Although Hirsch believed that no mathematic expression can be found for the extent of the aërial convection of smallpox, yet the experience of recent epidemics in the British Isles proves that its *striking distance* is considerable, certainly much greater than that of typhus fever. A local outbreak in Sheffield in 1887 and 1888 afforded an

opportunity of reducing the facts to a mathematic expression. According to A. Wynter Blyth, the influence of the Sheffield Hospital could be distinctly traced for a circular distance of 4000 feet. Whether the contagious particles are conveyed by the air itself, or by the medium of the common household fly or other insects, the important fact remains that the infection can strike at a considerable distance, though with less certainty as the distance increases from the infective center or focus of the disease. F. W. Barry, Inspector of the Local Government Board for England, found the following percentages of households attacked at successive distances from the Sheffield Hospital :

0–1000 FEET.	1000–2000 FEET.	2000–3000 FEET.	3000–4000 FEET.	ELSEWHERE.
1.75	0.50	0.14	0.05	0.02

At Bradford, in 1893, Arnold Evans confirmed Dr. Barry's conclusions, but he went further. A study of the direction of the prevailing winds throughout the year 1893 supplied him with evidence strongly confirmatory of the view that the poison was conveyed aërially direct from the wards of the hospital. Dr. Evans selected a one-mile area around the hospital and divided it into quadrants by drawing radii to north and south, to east and west. He found that in the northeast quadrant 7.06 % of the houses were infected ; in the northwest quadrant, 2.40 % ; in the southeast quadrant, 5.28 % ; and in the southwest quadrant, 2.93 %. The percentage of infected houses in the special zone east of the hospital was 5.6, compared with 2.9 on the west side. These figures are easily explained by the fact that westerly winds prevailed on two hundred and fifty days in the year, easterly winds on only eighty-three days. During the first half of the year, when easterly winds were more common than during the second half, the proportion of cases occurring on the western side of the hospital was relatively greater than during the remainder of the year, when east winds were less frequent.]

The contagiousness is, however, by no means dependent on the existence of the exanthem, as smallpox has been repeatedly transmitted to the healthy before the eruption appeared (in the initial period), and even toward the end of the period of incubation. Even in those interesting cases of variola sine exanthemate, which are characterized by the absence of a typical eruption, there is danger of infecting others, and this danger is also present during the healing of the exanthem as long as crusts and scabs are found on the body of the convalescent. It follows from all that has been said that smallpox is infectious by means of a volatile contagium, in every stage of the disease (without exception), but that the different stages, of course, show quantitative difference in this respect.

A fact which, for the pathogenesis of variola, is of scarcely less importance than the volatility of the contagium (or its transmissibility through the air) is its power and tendency to settle in the goods and furniture surrounding the patient and to cling to these persistently. Objects of loose texture and rough, uneven surface are by their physical construction best adapted to serve as shelter for the smallpox virus, and especially, of course, if they, like the body-linen and bed-clothing, are in direct contact with the patient; yet even articles at some distance, such as cushions, carpets, tapestry, etc., also shelter the poison. The contagium clings less readily to smooth and compact objects (made of glass, porcelain, metal, and wood). Though not entirely safe, they are therefore decidedly less dangerous (or susceptible), provided, of course, they are not directly soiled with the smallpox secretion. The danger that the disease may be effectively spread by means of lifeless material of the above-mentioned kinds needs to be emphasized all the more, since these objects, after removal from the neighborhood of the patient, retain the power of carrying the infectious material and distributing it to those who are susceptible.

To the list of highly susceptible things [fomites] belong, as is readily understood, the clothing and hair of the head and beard of those persons who remain in the neighborhood of the patient and attend to his wants (the friends, the nurse, and the physician). These persons, if not predisposed, do not themselves take the disease, although directly exposed to the contagium. But they may be, unfortunately, by want of prudence, and frequently are, the intermediate carriers of the contagium, which clings to them or their belongings.

The bodies of those who have died of smallpox are also infectious to a high degree, and the disease has been quite frequently contracted by laying out the corpse, or making an autopsy, or even by mere attendance at the funeral. Whether the smallpox virus has simply remained adherent to or inherent in the body after death, or whether it has reproduced itself in the body for a short time after death, the same prudence is demanded in our dealings with the dead body of the smallpox patient as in our intercourse with the living.

The vitality of the smallpox virus, under proper conditions, is extraordinarily great. For instance, dried pus from a variola efflorescence may be inoculated years afterward with positive results. Also the above-named carriers of infection [fomites] (as body- and bed-linen, clothing, etc.), if kept from the air and from high temperatures, long retain their power of transmission, and may later cause the disease. This insidious character of the poison deserves attention, for it explains,

among other things, the occurrence of many primary cases of variola in times and places otherwise free from the disease. This fact also shows that the smallpox poison, although it originates from the body of a smallpox patient, can retain its existence in a latent form for a long time outside of the human body.

The smallpox poison may be received into the system in different ways. The effects of inoculation teach us that a superficial injury of the skin may serve for a place of entrance, but this is not the usual mode of infection. Whether the uninjured skin is permeable to the poison is more than doubtful. Earlier experiments made in the time of the inoculation experiments, prove that smallpox pus rubbed into a spot on the skin for some time may produce an infection; yet the question might be raised whether, in this procedure, the superficial portion of the protecting epidermis was not rubbed off. The usual and natural mode of reception of the virus is undoubtedly by inhalation, in which the mucous membranes of the nose, pharynx, and upper air-passages, and eventually also those of the deeper portions of the respiratory tract, serve for entrance of the poison. Whether the uninjured mucous membranes are permeable, or whether a defect of the epithelium is necessary in order that the contagium may penetrate, cannot be directly decided; but probably the contagium attaches itself to the uninjured mucous membrane as, otherwise, natural infections would not be so easy and frequent. Finally, in many cases, infection by way of the digestive tract is possible, as infection with variola has been repeatedly brought about by the idiotic experiment of intentionally swallowing the smallpox pus. That a similar influence may be exerted unintentionally, by the accidental introduction of the pock-material into the mouth and stomach, cannot be denied. However, the digestive apparatus probably plays no important part in the natural genesis of the disease.

The preceding review embraces in reality only that part of the etiology of variola which could be empirically selected from the epidemiologic facts. It gives, to speak briefly, the more important external conditions under which the specific virus of variola can exert its pathogenic influence, and, according to experience, does exert it. The question of the real nature of the poison of smallpox has not been directly touched upon, and I will now discuss it briefly.

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PARASITOLOGY OF THE SMALLPOX VIRUS.

Our scientific observations on the virus of smallpox long since resulted in the idea of a contagium vivum (or animatum). The corresponding teaching of the etiology of infectious diseases in general (and especially of the contagious diseases) is far older than its actual proof in individual cases by modern bacteriologic methods. This idea owes its birth especially to variola, which, historically considered, is of essential and fundamental importance for the whole theory of contagium vivum and its later generalization. The experiment of inoculation made over and over again, showing that a minimal amount of the contents of a smallpox efflorescence is generally sufficient to produce a whole new case of smallpox, as well as that a whole epidemic of variola may easily arise from a single case, admits of no other explanation than that the cause of smallpox has in a high degree the power to reproduce itself, and, according to experience, reproduction (or proliferation) is a power inherent in living beings. The view that the origin of smallpox must be connected with a living being, not, indeed, visible to the unaided eye (because too small), but existent and endowed with pathogenic properties, appeared not only the most plausible, but even the only possible explanation. It was, indeed, for variola first among all infectious diseases that the theory was made and of which from the beginning it was postulated.

With the actual discovery of a specific pathogenic micro-organism for a number of other infectious diseases (anthrax, relapsing fever, etc.) in the present age of bacteriologic triumphs, the hypothesis of the existence of a micro-organism of variola as the cause of the disease had attained the highest degree of probability ; it was now important to find in the contents of the variola pocks or in the blood of the variola patient a living organism peculiar to it and especially characteristic of it. Earlier attempts with this in view had not been lacking, for the oldest dates back into the eighteenth century. But they, on account of the poverty of the methods, had, of course, no result. More and better results were to be expected from the new and developing technic in bacteriologic fields, and, on the basis of historic reverence, the task of seeking a cause for variola seemed alluring. Indeed, during the last

ten years, and down to the present time, a large number of very emi-
nent investigators in this special field of microscopy have labored most
eagerly in the search for the micro-organism of smallpox (see the ap-
pended bibliographic references), but the results have hardly corre-
sponded to the expectation. To be sure, very often in microscopic
sections of smallpox efflorescences, and not infrequently in preparations
of their contents, micro-organisms (namely cocci) have been detected by
the proper staining methods (hematoxylin and methyl-violet); but all
these specimens were lacking in the uniformity and constancy necessary
to enable us to decide that they were related etiologically to variola.
It seemed, however, significant, although only from the negative aspect,
that the clear (not yet turbid) contents of the variola pocks in the
vesicular stage, and also the clear vaccine lymph, in spite of their
evident infectious character, should nevertheless be often entirely free
from parasitic forms. This circumstance seemed to show the inade-
quacy of the usual methods of investigation to the special purpose in
view, and demanded some other technic. (See below.) It also seemed
remarkable that, in the contents of the eruption in the pustular stage
(pustules), the different species of ordinary pyogenic germs were easily
demonstrated—Staphylococcus aureus, citreus, and albus (P. Guttmann),
or Streptococcus pyogenes (Garrè), in 3 very severe cases of variola. As
these ordinary pus cocci are to be met in pus wherever it originates,
their presence in the suppurating pock probably merely shows that in
variola they are the cause of the secondary suppuration. Of course,
they cannot be considered as at the same time the true or even the chief
cause of variola. An important deduction from this finding is that
suppuration, although very frequent and almost universal in the usual
course of variola vera, is really nothing but a complication of the dis-
ease or an accident caused by a different but always accessory or mixed
infection.

Very recently, two essentially different publications have appeared
on the nature of the exciting cause of variola. One of these works
(Buttersack) comes from the Imperial Health Office at Berlin, under R.
Koch, and brings forward very remarkable statements concerning the
existence of thread-like and spore-bearing forms in vaccine lymph and
also in the fluid contents of fresh variola pocks. Only clear (not tur-
bid, purulent) material was used for the investigation, and a procedure
totally different from those hitherto used (investigation of air-dried
preparations, without addition of a fluid) was used in order to make the
forms which otherwise are invisible and unstainable optically different,
and hence microscopically recognizable. For further details, we must

refer to the original work. It may be mentioned here, however, that the threads in question, according to Buttersack, are regularly found in the clear vaccine and variola lymph, while in other clear exudations, as in the contents of the blisters from burns, they are not to be found.

However tempting it might otherwise appear to view in Buttersack's threads and their derivatives (spores?) the long but vainly sought for specific cause of variola and vaccinia, yet the photographs accompanying the work are, in my judgment, by no means convincing. Other observers, too, partly by way of testing the work (Landmann), have entirely rejected the threads (and spores) in question, and have expressed the idea that they are really artificial, the result of the somewhat detrimental treatment of the preparation under examination.

The other important work in this much-disputed realm of microparasitic investigation comes from the pen of L. Pfeiffer, and forms the continuation as well as the résumé of the earlier publications of this well-known author. At the same time, it contains, which is important, an acknowledgment and confirmation of the results obtained by Van der Loeff and von Guarnieri. As the common cause of the variola process and the vaccination process, L. Pfeiffer distinguishes peculiar, sharply defined sporozoa (amebæ) with special biologic properties (*Cytorrhyctes variolæ*, after Guarnieri). This parasite, according to Van der Loeff, is found regularly in the blood of variola patients during the initial febrile stage of smallpox, also in the blood of vaccinated children during the febrile stage of vaccination, and also in the blood of vaccinated calves during the corresponding period. During its stay in the blood, it is about one-fourth the size of a human red blood-cell, shows active motility with formation of pseudopodia, and, while floating freely in the blood, appears possessed of a lashing flagellum, which may be made visible in Löffler's flagellum stain. Unlike the sporozoa of malaria, it does not penetrate the red blood-corpuscle, but clings to it or flows actively around it; with the decline of fever, the parasite disappears from the blood; then it appears at the time of the outbreak of the exanthem on skin and mucous membranes in the places of the coming smallpox efflorescences (L. Pfeiffer). This change of location is probably brought about by an embolic process; it is dependent also, however, on a change in the biologic and morphologic properties of the parasite which fits it for its new location. The further course of development, according to L. Pfeiffer, is as follows: After entering the skin, the stranger, which, as cause of the variolous pocks, has to play a pathogenic rôle, makes its way from the corium to the epithelial cells of the prickle layer (Rete Malpighii), which it penetrates. Unlike many other parasites which

especially attack the nucleus of the cell (karyophagic parasites), the *Cytorrhyctes variolæ* leaves the nucleus as such untouched and nourishes itself exclusively on the protoplasm. While it continuously increases in size, and the protoplasm diminishes, the nucleus of the prickle cell thus attacked is pressed more and more to the side (the cell wall), becomes flattened, and finally is indented on the side toward the parasite ("niche-like"). This course of development of the parasite in the cells taken by it as hosts may be more easily traced in the more transparent cells of the middle layers of the corneal epithelium than in the prickle cells of the epidermis. If we inoculate (Guarnieri) clear vaccine or variola lymph into the living cornea (of a rabbit's eye), in two days changes appear which are altogether analogous to the changes in the cells of the epidermis in the prepustular stage of variola. In this way, however, material is obtained for an easier and more convenient observation of the parasite. At about the time above mentioned, this parasite may be seen as a small body which has penetrated the epithelial cell and is lying near the cell nucleus. It increases in size in the interior of the cell at the cost of the protoplasm of the cell, and finally proliferates. The method of proliferation is twofold : simple division of the parasite after preliminary division of its nucleus and cystoid change of form with endogenous spore-formation and subsequent segmentary fragmentation. The later fate of the free spores has not yet been exactly ascertained; but L. Pfeiffer thinks that they resemble in size those corpuscular elements which Chauveau obtained by filtration of the clear contents of the vesicles. It may be possible that the two elements are indeed identical, in which case it is easy to explain why no fully developed micro-organism has hitherto been found in the clear lymph in spite of its evident infectious character.

Only the briefest abstract of the results of the investigations of Van der Loeff, L. Pfeiffer, and Guarnieri can be given here. They, of course, need further and more general confirmation. But they possess the greatest scientific interest, both because of the conclusive form in which they were presented by L. Pfeiffer in his last publication and because of the complete correspondence of the results of the three investigators. The hope is therefore well founded that by these works a decided advance has been made in our knowledge of the special nature of the smallpox virus and the vaccine virus, and the future will teach the rest.

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PATHOLOGY.

IN giving a concise description of the pathology of smallpox, we encounter the difficulty that the different cases of variola vary so much, and that all imaginable intermediate grades are found between the lightest and severest forms of the disease, even in its regular form. Besides these differences in intensity of the disease, there are also qualitative differences in symptoms and course, which increase the manifold clinical characteristics in particular cases. It follows from what has been said, that in spite of our effort to treat all these modifications fairly, the description which follows cannot lay claim to being perfect, and we cannot deny that it is at times schematic in character.

As these differences are fewer in the beginning of the disease than in its later course, so the difficulty mentioned above is greatest in describing the later stages of smallpox. Indeed, we may be permitted, without much damage to the truth, to describe together not only the stage of incubation, but also the initial stage of the disease in the great majority of all forms of the disease, and to consider separately the infrequent variations from the rule. On the other hand, a separate description of the various clinical modifications of variola is given for the later stages; that is, for the conditions existing during the appearance of the eruption and after its complete development. The plan of the following description may, therefore, be criticized in this respect.

SYMPTOMATOLOGY AND COURSE.

STAGE OF INCUBATION.

By stage of incubation in infectious diseases we mean the time from the entrance of the specific pathogenic agent to the appearance of the first typical symptoms of the disease. This period, also called the "period of latency," lasts generally ten to thirteen days in variola; very rarely more, even to fifteen days; more frequently less, five to ten days, especially in the very severe, primarily hemorrhagic cases of so-called purpura variolosa (Zuelzer).

Not every case of variola can be used in fixing the period of incubation, as very often neither observation nor the history of the cases gives the time of infection. Nevertheless both in recent and earlier times there have been sufficiently numerous and exact determinations as to the dura-

tion of the stage of incubation, all of which agree on ten to thirteen days as the usual duration. The twelfth day after infection seems to be the one on which the typical symptoms of the disease most frequently appear.

The cases of variola after inoculation follow a special rule ; in these, according to the numerous and exact observations of the eighteenth century, the first local symptoms of the disease appear at the site of inoculation far earlier (toward the end of the third day or on the fourth day), and the general symptoms of the initial period (high fever, etc.) also appear earlier than is usually the case in naturally acquired variola. We do not know the true reason of this difference in the duration of the stage of incubation, which is evidently dependent on the place of entrance of the virus.

The more detailed description of inoculated variola, for theoretic as well as for practical reasons, is given later (in the section on "Vaccination").

Whether, during the period of latency, typical changes take place in the body of the infected is unknown and is certainly not demonstrable. Such changes must certainly be assumed theoretically on the entrance of the variola germ. They consist probably of a further development and proliferation of the germ up to the time when it suddenly develops its poisonous influence. In what portion of the infected body these living predecessors of the contagium are during this stage, and how they proceed to the next location, is unknown, and needs further investigation.

The condition of the patient during the stage of incubation is usually entirely undisturbed. In a minority of the cases certain slight complaints are expressed, as of lessening of the appetite, languor, headache, etc., which may be considered as real prodromal symptoms or which may be purely accidental. More suspicious, in the prodromal connection, is the occurrence of pain in the back toward the end of the period of latency, which is also noted now and then in the histories of patients. This symptom is probably not accidental, but is an expression of the specific variolous infection, as it is numbered among the most characteristic and most frequently complained of symptoms of the period following the first or the initial stage of variola (compare later).

Finally, it may be mentioned that Obermeyer, during the great smallpox epidemic of 1870 and 1871, frequently observed, during the last days of the period of incubation, symptoms of mild pharyngitis, redness and swelling of the uvula and tonsils, which, in view of its later exacerbation during the initial stage, must be considered as prodromal, although it is by no means constant.

If the subjective condition of the patient during this preliminary stage

is quite normal, this period of latency changes very suddenly into rather severe sickness after the completed incubation of the contagium. Also when the very slight prodromata already mentioned exist, the passage into the initial stage is quite abrupt, so that there can be no doubt concerning the day on which the disease really begins.

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INITIAL STAGE.

By the initial stage of variola is generally understood the time between the beginning of the first distinct symptoms of the disease and the first appearance of the eruption on the skin. The regular and characteristic symptoms observed during this time are collectively characterized as initial symptoms of variola. They are found alike in the mild and in the severe forms of smallpox, and are usually not lacking even in the irregular forms of the disease. Variola, as a disease *sui generis,* is recognized by the constant presence of a fixed and limited initial stage of peculiar characteristics even more certainly than by the smallpox exanthem. The eruption may be wholly absent (variola sine exanthemate) or may be present in a wholly atypical form (purpura variolosa), and yet these anomalous cases may be cases of true smallpox. On the other hand, there is hardly a case of variola in which, after the infection and period of incubation, the eruption is not preceded by an illness of definite duration—the initial stage.

This period usually lasts three days, and generally toward the end of the fourth twenty-four-hours' period the first traces of the exanthem appear on the skin. Rarely a shorter (two days) and still more rarely a longer (four days) initial period has been observed. The former, the shorter period, occurs most frequently in children; besides this, however, a specially severe form of smallpox, variola confluens, is not infrequently indicated by a precipitated eruption of the exanthem (Sydenham, van Swieten). No other relations exist between the duration of the initial stage and the character of the subsequent eruption; rather, from the intensity of the initial symptoms, certain prognostic conclusions may be drawn; but these have a definite value in only one direction (compare the following).

The initial stage may be light or severe, the severity differing in different cases. It should be especially noticed that the severity of the initial stage does not of itself indicate anything about the severity of

the further course of the disease, but that many cases of varioloid (the light form of variola) are introduced by violent initial symptoms. Individual peculiarities, especially an irritable condition of the nervous system, play an important part, and often, according to my experience, cause, in the beginning of the disease, apparently threatening symptoms. On the other hand, a mild initial stage with absolute certainty excludes a severe subsequent course, especially a variola confluens and a variola hæmorrhagica. Therefore no prognostic value can be assigned to a severe initial stage, but a mild initial stage indicates a favorable prognosis.

The course and symptoms of the initial stage are usually as follows: The disease begins in most cases very acutely; a rapidly increasing feeling of general weakness and malaise takes possession of the patient; dysphoria and adynamia soon accompany this, shown very clearly in adults by headache, dizziness, and a narcotic benumbing of the sensorium. Although, in mild cases, this apparent toxemic disturbance is somewhat less intense, yet even in such cases it makes itself plainly perceptible; in severe cases, on the other hand, its progress is so powerful that the patient is entirely overcome by it. General convulsions are not infrequently an initial symptom in young children.

It results from such initial symptoms, and from the rapidity of their invasion, that most variola patients are soon unable to drag themselves about. One who has a home and a bed of his own usually seeks them as quickly as possible. Vagrants, on the other hand, who are attacked by the initial symptoms of variola during their wanderings reach, if possible, a needed shelter in the immediate neighborhood; or, if this is impossible, they remain in the open air and lie down in the fields or on the outskirts of cities. If such individuals are placed on their feet, they fall from weakness; this helplessness, the staring look, the stammering tongue, and the often occurring *status delirans* naturally suggest the idea of intoxication. In this supposed condition, they are taken (instead of to the hospital, or, better, to the isolation house for smallpox suspects and smallpox patients) to the police station, often to the injury of many others, until the fatal mistake is discovered with the appearance of the eruption.

Simultaneously with the appearance of the severe general disturbance, the body-temperature begins to rise, and, with few exceptions, a high fever soon develops. This is sometimes introduced by one severe rigor, oftener by several chills, which in both cases are soon replaced by an ever-increasing sensation of heat. The body-temperature on the first day, and even in a few hours, reaches a considerable height (40° C. or thereabout), and frequently rises still higher, with scarcely noticeable remissions in the morning hours, so that on the second and third days of illness (before the beginning of the eruption) a maximal fever height

of 41.0° to 41.5° C. is not unheard of.   This high fever, of a subcon-
tinuous character with rising tendency, which lasts during the whole
initial period of variola, is called, to distinguish it from the later sup-
purative fever of severe cases, the initial fever of variola, and intro-
duces grave and mild cases of smallpox alike; among all the phenomena
of the beginning of the disease, none furnish so little prognostic indica-
tion concerning the further course of the disease as the height of the
initial fever; for while varioloid not infrequently shows a very consider-
able initial temperature, the fever in the very worst form of variola—
the purpura variolosa—is not usually at all excessive.

In correspondence with the fever and increase of temperature, the
pulse-rate and the rate of respiration also increase in all cases from the
beginning; so that the pulse may not infrequently reach 120 and the
respirations may number 36 per minute.   In children, women, and
excitable individuals, these influences of the fever are seen still more
frequently, as is observed in other acute febrile diseases.

The pulse varies in volume.   Most frequently in individuals of sound
constitution, the pulse during the initial period is full and the arteries
are somewhat distended.   In especially grave cases, on the other hand,
as in cases of purpura variolosa, the pulse, early in the disease, becomes
small and weak, then usually irregular and intermittent.

The skin in most cases feels burning hot (*calor mordax*) and is gen-
erally dry.   Perspiration in this period is rarely perceptible; whether,
as Trousseau thought, its presence indicates a favorable prognosis is
more than doubtful.   The cheeks appear, as a rule, bright red; the
conjunctivæ and lips are injected.   The tongue is broad, shows indenta-
tions from the teeth, and is covered, on nearly its whole upper surface,
with a thick, oily, yellowish-white coating.   Corresponding to this, a
fœtor ex ore makes itself offensively noticeable, and the symptoms of a
marked pharyngitis (redness and swelling of the follicles) are now gen-
erally present (compare stage of incubation), with a certain degree of
dysphagia.

Appetite and thirst show the changes which usually occur in acute
febrile infectious diseases, the latter being above and the former far
below the normal.   Besides the complete anorexia, nausea is nearly
always present, and often, especially in severe cases, distressing retch-
ing, and even repeated spasmodic vomiting; attacks of hiccup (sin-
gultus) are not infrequent.

Real normal sleep is, with few exceptions, entirely lacking; instead
of it, delirium often occurs in the further course of the disease, in con-
junction with the intoxication symptoms of the invasion.   The de-

lirium, which is sometimes of the quiet kind, and sometimes noisy and violent, is observed with great regularity, of course, in alcoholics, but is so little a symptom belonging exclusively to them that it may be counted as one of the pathognomonic symptoms of variolous blood-poisoning. Actual coma, on the other hand, is very rare; it occurs in connection with certain other alarming symptoms—as irregular, stertorous breathing, moist râles in the chest, great exacerbation of the pulse (quick, small pulse)—only in quite exceptional cases of very severe infection which end fatally in the initial stage (*variola siderans*).

If the sensorium, in spite of some delirium, remains, as usually happens, so far normal that the patients answer questions slowly and voluntarily express their complaints, then the pain in the head regularly forms one of the chief burdens of their complaint. This pain is sometimes more pronounced in the forehead and temporal regions; sometimes it is diffuse, and is often so violent that patients who are delirious and somewhat stupefied grasp at their heads. In connection with the high fever and jactitation of the patient, such a symptom should conclusively prove that variola in the initial stage may simulate a meningitis.

The feeling of dizziness which, before the patient was confined to his bed, manifested itself in walking, and reeling about, does not leave him when he is in bed and is increased when he attempts to rise. Among other phenomena of cerebral irritation, we may mention flashes before the eyes, or so-called seeing of sparks, and roaring in the ears as frequent accompaniments of the headache and dizziness.

Dragging or boring pains in the extremities are complained of by many patients. Still more regularly a feeling of painful separation arises in the joints (the shoulder, hip, knee, elbow, etc.). If these phenomena are very prominent, the picture of the disease resembles rheumatism or a septic affection, and may even be confounded with these.

To the noteworthy, because most frequent, initial symptoms of variola may be added a more or less intense lumbosacral pain. This symptom has a special significance in the diagnosis of an initial variola because it is relatively rare in other febrile conditions, and is almost never present to the same degree. In variola, on the other hand, the so-called loin pain (localized in the loins rather than in the sacral region) is entirely lacking in only a few cases, and these are quite mild, rudimentary cases. In the other cases, the severe ones especially, but also in many of the mild ones, the symptom is not only present, but is so marked that the patients complain of it spontaneously, or at least

when one raises or moves them. The loin pain is in general especially intense in those extremely bad smallpox cases, which later become hemorrhagic (or purpura variolosa), and still more so in the primarily hemorrhagic cases. From all that has been said, we may see the importance of these symptoms as regards diagnosis and also prognosis, at least so far as the extreme differences in intensity are concerned.

Authors do not agree concerning the cause of this initial lumbar pain; while some regard it as a pure (nervous) intoxication symptom, others ascribe it to congestion of the kidneys or of the membrane of the spinal cord, or, finally, to hyperemia of the hip-bone marrow itself. Possibly there may be hyperemic changes in all the parts named and in hemorrhagic variola, also precursory hemorrhages in the same ,which may have more or less to do with the origin of the symptom. (Compare Pathologic Anatomy.)

Abnormal sensations may be mentioned among the rarer epiphenomena : now and then pain in the neck is present, which, when it exists in connection with the regular severe pain in the head, makes it especially natural to confound the initial variola with meningitis. A wretched feeling of oppression in the chest and a painful sensation in the precordia are somewhat more frequently observed. These two latter phenomena are more frequently lacking than present; they seem to favor especially the variola cases which later run a severe course (especially hemorrhagic), and therefore indicate, on the whole, an unfavorable prognosis.

The physical examination of the thoracic organs shows nothing special in regard to heart dulness and heart tone, lung sound, and respiratory murmur. Now and then slight bronchitic signs (scattered rhonchi, some râles) may be perceived on auscultation, but this is the exception rather than the rule.

The liver also presents nothing unusual on examination. The spleen, on the other hand, though not constantly, yet very frequently, is distinctly swollen, and perceptible by percussion and palpation (Friedreich). Curschmann thinks that the splenic tumor of the initial stage is present only in the future variola vera, but not in varioloid, and he, on this account, ascribes to it a prognostic value. On the other hand, the splenic tumor is by no means generally present in severe cases, for, strange to say, the gravest form of smallpox—purpura variolosa—is, it appears, constantly characterized by absence of a splenic tumor. (Compare Pathologic Anatomy.)

The bowels are generally constipated, and remain so during the further course of the disease; a normal stool is rare, and diarrheal evacuations are still more rarely observed. Of the bloody stools

which occur in cases of purpura variolosa, we will speak under that heading.

The urine, as would be expected after the high fever, is dark and scanty, and not infrequently albuminous (so-called febrile or hematogenous albuminuria). There is usually no sediment in it at this time. Hematuria as a symptom of the general hemorrhagic diathesis also occurs, with the other hemorrhagic symptoms, in purpura variolosa.

In women the condition of menstruation in the initial stage of smallpox is important. It happens quite frequently that, although the regular time has not arrived, the menstrual flow begins with the commencement of the initial stage of the disease and is unusually profuse.

This is especially characteristic for variola, so that, in conjunction with a sudden appearance of high fever, and other general symptoms of the disease, it can be used for an early diagnosis. It is also characteristic of the disease that pregnant women, if attacked by variola, are prematurely delivered or abort, according to the stage of pregnancy. (For intra-uterine infection of the fetus in such cases and congenital variola, compare Etiology and Pathology, above.)

In concluding this account of the symptoms of the initial stage of variola, I will add a few words concerning the interesting as well as diagnostically important initial eruption in smallpox patients. Attention has been especially called to its occurrence in recent epidemics; F. v. Hebra and Th. Simon have made very careful observations of this eruption and its relation to the other processes of variola. Not a few very excellent observations and descriptions were also given in former times, yet the cases were, as a rule, wrongly interpreted, and regarded as a combination of variola with measles and scarlet fever. The frequency of this peculiar skin affection, which appears on the surface of the body during the initial period before the appearance of the true smallpox exanthem, varies exceedingly, and the special "*genius epidemicus*" has gained prominence on its account. In what the force consists which at times brings about this epiphenomenon is perfectly inexplicable. Two essentially different forms of the initial exanthem in variola are to be distinguished clinically : Differences are noted in form as well as in location, in the outset as well as in the duration of the skin changes, and even in prognostic relations the two forms are peculiarly unlike. One, and that the far more frequently observed, form of the initial exanthem is the roseolar (Hebra), also called "measles-like" (although the typical papular form of the exanthem of measles is never found); it is also identical with the "rash" described by English writers. This exanthem makes its appearance on the second day of the initial stage (rarely later

or earlier), and has usually entirely disappeared from the skin in little more than twenty-four hours; in no case does it last until the appearance of the true variola eruption. It consists of rose-red macules, just at the level of the skin, whose redness disappears on pressure, but quickly reappears; some of them are small, of the size of a lentil, and round, while others are larger and of irregular contour. These macules usually appear first on the face, but then extend to the rest of the body and are especially numerous on the extremities. In most cases they reach their maximal intensity in a very short time (a few hours), and then, as already remarked, disappear somewhat more slowly than they appeared, and leave no trace. From all that is known, it appears that this rash is due not so much to an exudative inflammation as to a pure hyperemia of the skin of vasomotor origin, as otherwise the extremely fleeting nature of the exanthem could hardly be explained.

The roseolar initial eruption is found far more frequently in varioloid than in severe cases of variola. A favorable prognostic indication for the further course of the disease is therefore, not without reason, assigned to it. My own quite numerous observations on this point confirm this decision, as I have seen this form of initial exanthem almost exclusively in cases of varioloid.

The second and much rarer form of initial exanthem of variola is quite different from the first; it begins earlier, generally on the first day of the disease, and even sometimes precedes the fever and other initial symptoms (W. Bernouilli, Curschmann). In contrast to the initial erythema of the first kind (the roseola variolosa), it is called by many "variolous initial exanthem," or initial erythema of the second kind (Hebra); it is also called "scarlatinous initial exanthem" because of its dominant color, and also "hemorrhagic erythema," on account of the capillary hemorrhages which regularly occur in the area of its distribution. This area of distribution presents the following special peculiarities: It occurs mostly (Hebra) in the lower half of the abdomen in a region which is rather sharply limited above by a transverse line at about the level of the umbilicus; further, also (excluding the genitalia) on the inner surface of both thighs to the knee; the surface of the skin in these regions is of a dusky burning red color, as in *scarlatina lævigata*, and presents numerous smaller and larger purple-red macules with irregular borders (arising from hemorrhages). If the patient lies with adducted thighs, then the whole presents a triangular figure of the red color mentioned above, the base of the triangle being directed toward the trunk, the somewhat rounded lower angle lying a little above the level of the knee. Following Th. Simon, the region mentioned is usu-

ally called the "femoral triangle" (Schenkeldreieck), and the exanthem thus localized is called the "erythema in the femoral triangle." At other times, but more rarely, this triangle shows on both sides lateral extensions upward, and the erythemato-hemorrhagic region covers to the right and left the sides of the trunk, the axillary regions, a part of the inner surface of both arms, and the portions adjacent to the axillary space of the anterior region of the chest wall on both sides (" shoulder triangle "). Sometimes the shoulder triangles exist alone or the erythema appears chiefly on one side in these upper regions of the body (" unilateral shoulder triangle ").

The scarlatinous " erythema variolosum " lasts, as a rule, until after the beginning of the true variola eruption and recedes slowly. The numerous hemorrhagic spots (petechiæ and ecchymoses) pass through the usual changes in color, and, of course, therefore last especially long. A subsequent desquamation of the skin in the affected parts does not, however, take place. (It is thus distinguished from true scarlatina.)

It is remarkable that a certain relation of exclusion exists between the areas of distribution of the hemorrhagic initial erythema and the subsequent true variola exanthem ; however abundant the smallpox eruption may be in the cases in question, the parts of the body affected by the initial erythema are either entirely spared by the real pocks or are very sparingly covered by them (Trousseau, Hebra). The reason for this peculiar relation is as little understood as is the nature of the hemorrhagic erythema. [It is probable that the devitalized state of the blood in the area of the initial erythema interferes with the development of the true variolous eruption. There is doubtless a condition of bacterial thrombosis.]

The striking and noticeable peculiarities in the distribution and limitations of the hemorrhagic erythema must naturally suggest a trophoneurotic influence; but it would be decidedly premature to say anything more definite at this time.

The hemorrhagic erythema is said by some (Hebra) to occur in women more frequently than in men, and, in contrast to the roseolar erythema, to indicate an unfavorable prognosis concerning the further progress of the disease ; but both these assertions are energetically disputed by others (Th. Simon).

My own observations, which happen to have been very limited in this special region of the pathology of smallpox, do not indicate any controlling influence of sex, but, on the other hand, they do suggest a warning concerning the prognosis. The few cases of this kind observed by me died, with one exception, in the suppurative stage of the disease.

This finishes what it is necessary to say concerning the initial stage of variola. Usually toward the end of the third nightly febrile exacerbation—that is, for the most part, late in the evening or on the following morning, but sometimes sooner and only rarely later (during the fourth day of the disease)—indications of the peculiar smallpox exanthem appear on the skin, and thus the patient enters the stage of eruption.

I will subsequently speak briefly of *variola sine exanthemate*, and in the same connection of the light form of smallpox (varioloid) with which the *variola sine exanthemate* corresponds so far as the decline of the fever and the favorable prognosis are concerned. As almost imperceptible transition stages exist between the cases with sparingly developed varioloid exanthem and those with none whatever, this seems to me the most logical classification of the subject.

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FURTHER COURSE OF THE DISEASE.

With the beginning of the period of eruption, the further course of the different forms of the disease becomes much more divergent than is the case in the period of incubation and in the initial stage. A special description of the chief clinical modifications of variola seems therefore proper, as noted in an earlier part of this treatise, and we will begin with the regular type of the disease, the variola vera (or simply variola).

Variola Vera.—By variola vera we understand a fully developed but not otherwise complicated form of smallpox. In distinction from varioloid, all those cases are so called in which to the subsequent eruption and development of the exanthem is added a more or less decided suppuration of the separate well-developed smallpox efflorescences, joined with more or less severe general symptoms (namely, marked suppurative fever); in these also, if life is preserved, certain stigmata, especially true

smallpox scars, remain permanently on the skin as remains of the previous intense local process. Before the introduction of vaccination, these formed the majority of all cases of smallpox in most epidemics, although with all imaginable degrees of intensity. Now they occur mostly in those who have not been vaccinated or in whom revaccination has not been at all or not well attended to. From variola confluens, the simple variola vera (or discreta) is distinguished by the fact that in this form there is no or only a slight blending of the individual smallpox efflorescences in the stage of suppuration, as well as that only small, round discrete scars are left. Among all the forms of smallpox, variola vera is especially characterized by the duration of the period of eruption and the manner in which the exanthem is usually distributed over the skin, and, most of all, by a typical behavior, so that on this account it deserves to be first mentioned in this description.

Period of Eruption and Development (**Efflorescence**).—*Symptoms in the Skin and Mucous Membranes.*—The eruption, which usually begins toward the end of the third day of sickness (compare the earlier statements) generally advances slowly in variola vera and lasts usually about three days. Hence it is evident that in the regular form of the disease about six days intervene between the beginning of the initial stage and the time when the smallpox efflorescences are distributed over the whole surface of the body. The period of development of the rash following its first eruption—that is, the period of conversion of the original papules into vesicles with clear contents—usually consumes two days, after which, on about the eighth day of the disease, suppuration of the pocks begins.

The manner of distribution of the smallpox exanthem over the surface of the body in variola vera is especially characteristic, in so much that its anatomic topography is far more regular than in the other forms of smallpox.

The face and head are almost always attacked first; then, gradually descending, the trunk, and last the extremities, so that the variolous pocks in the three regions named appear respectively on the first, the second, and the third day of the period of eruption. Subsequent batches of spots may appear in the regions already attacked during the three days, but they are not numerous, and usually none appear after the end of the characteristic time of the general eruption. At this time, toward the end of the sixth day of illness, the whole surface of the patient's body is more or less thickly covered with discrete pocks, which become vesicular on the face and head while those on the rest of the body are still papular.

The pocks in variola vera are, as a rule, thickest where they appear first, hence on the face and head; in the portions later attacked (trunk and limbs) the pocks are fewer, with certain exceptions which I will name. An especially abundant, and at the same time premature, eruption is not infrequently observed on parts of the body which, before the beginning of the variola process, had been affected by mechanical or chemical irritation; this happens not only in cases of variola vera, but also in varioloid. Such local collections of the exanthem are sharply contoured from the surrounding unaffected skin, and are striking because of their peculiar localization and configuration. Both localization and configuration are so strictly limited to the areas of distribution of the previous mechanical or chemical irritation that they often give a clue to its nature.

Thus, in male patients we often see a thick stripe of variola papules on that region of the neck which is constantly irritated by the pressure and rubbing of the collar. Still oftener we see in women a narrow ring of pocks on both limbs in the region of the garters. The same thing has been observed around the waist, etc. I was struck recently by a case which came under my own observation; the varioloid eruption was very sparing, but numerous and closely crowded pocks appeared in a limited zone of both thighs, a stripe of hand-breadth running down to the knee. The patient was a young traveling journeyman, whose trousers fitted him badly and had irritated the parts mentioned symmetrically on the two sides. The eruption was at least twelve hours earlier in these two regions than even on the face, and the patient was presented to the clinic as an interesting case of extensive *"herpes zoster cruralis bilateralis"* because of the peculiar symmetric arrangement and limitation of this premature eruption.

That the same phenomenon may be caused by chemical irritation as well as by mechanical is shown by many examples from the literature of the subject. Especially well known are the masses of eruption on parts of the skin to which vesicants have previously been applied or which have been painted with iodin. To this class belongs also the marked distribution of the exanthem on the hands and forearms of washerwomen and others who handle irritating fluids.

On the other hand, we often see individuals who have an abundant exanthem over the whole surface of the body with the exception of one or more large areas, which may be entirely free from the pocks or only sparingly covered with them. Under this heading we may place the already mentioned immunity of the so-called femoral triangle (compare initial stage), which is so often attacked by the initial erythema of the

second kind (or hemorrhagic initial erythema). In addition, it should be noted that, even though this femoral triangle has exhibited no initial erythema the variolous eruption may also be lacking, for which no sufficient reason has been advanced. Similar local immunity to the small-pox exanthem has been observed in a few cases in other parts of the body.

The individual pock (in the face as well as elsewhere) develops as follows : With slight itching and burning, isolated red points appear. These at first are of the size of a millet-seed or the head of a pin, are somewhat hard, and just perceptibly elevated above the level of the surface. These small papules gradually become harder and more prominent, and increase somewhat in breadth, so that in twenty-four hours they are of the size of a bean or pea. They become intensely red in color, but an area or zone of inflammation around each papule is not yet seen. In the face on the fifth day of the disease, and correspondingly later in the other parts of the body, vesicles with clear contents (smallpox lymph) begin to be found in the upper part of the papule, and extend to the breadth of the whole papule during the next two days, becoming constantly more tense from the increase of the contents (stage of efflorescence). Finally (in the face, usually on the eighth day of the disease) the previously clear contents of the vesicular pocks begin to become turbid and the transparent appearance to change to a light yellow, somewhat opaque appearance (beginning of the pustular stage).

Many, but not all, of the pocks show, at about this time of development, the so-called umbilication ; that is, a navel-like depression in the center, around which the surrounding surface of the vesicle is elevated like a wall. Among the umbilicated pocks are found many whose depression is penetrated by a hair, and which therefore correspond to the point of exit of a hair follicle with the sebaceous gland belonging to it. In other umbilicated pocks the latter peculiarity is wanting, while others which are penetrated by a hair show no distinct umbilication. The central depression—a very frequent and in many respects quite characteristic peculiarity of the pock in the vesicular stage or stage of efflorescence —has given rise to many investigations and discussions. That it has no necessary relation with the original canals of the skin is shown conclusively from what has just been said (compare under Pathologic Anatomy in the latter part of the work).

If one carefully pricks a smallpox vesicle at the side with a fine lancet, he will usually not succeed in completely emptying the fluid contents at one time ; it is almost always necessary to prick it several times, and even many times in different places. The same is almost always

true of the non-umbilicated vesicles. This shows that the vesicle consists not of a single chamber, but of several cavities, placed beside each other and separated by septa. The more minute investigation of excised pocks confirms this assumption, as will later be further explained. (See Pathologic Anatomy.)

An appearance and a behavior differing from those described are presented by the pocks on the palms of the hand and the soles of the feet, especially on the more callous portions of both. They appear in these situations as pale red macules surrounded by a zone of induration; they do not, however, as elsewhere, form definite papules, but persist as patches lying at the level of the general surface of the skin. Later, in the vesicular stage, these patches become dimly translucent, surrounded by a narrow red zone. If one pricks one of these patches in the center, he must, on account of the thickness of the epidermis, penetrate to some depth before reaching the lymph chambers in these quasi-subterranean vesicles.

Besides the skin, the neighboring mucous membranes are also attacked by the typical exanthem in variola vera. These pocks on the mucous membrane appear either simultaneously with those on the adjacent skin or a little earlier than these. The mucous membranes of the upper part of the body, corresponding to the skin of the head and face, are attacked earliest and most severely. The eruption appears especially on the mucous membranes of the mouth, nose, and throat, from which it may extend variable distances downward in the pharynx, larynx, and trachea, and even penetrate into the larger bronchi. Among the different portions of the mouth, the lips and cheeks, soft palate, and floor of the mouth are favored by the exanthem, in preference to the tongue and gums, although single pocks may appear on the latter, especially on the edge and lower surface of the tongue. An extension of the middle exanthem through the Eustachian tube to the middle ear, which was formerly assumed, seems in reality to happen just as seldom as such an extension from the skin of the deeper (bony) parts of the external ear or of the tympanic membrane (Wendt); the frequent disturbances in the region of the auditory apparatus in variola may be explained partly by the participation of the skin of the cartilaginous part of the external ear in the skin eruption, and partly in other ways, which will be described later. The same negative result applies to the nasal duct, and, with rare exceptions (Hebra, Adler), to the conjunctiva bulbi; but, on the other hand, typical eruptions on the conjunctiva palpebrarum have been more frequently observed and accurately described.

The mucous membranes of the lower part of the body are, like the

skin in these regions, attacked later, and at about the same time as the skin. In these parts true pocks are formed only on the lowest portions of the rectal mucosa, next to the anus, and in females in the region of the vulva and vagina, as well as rarely at the urethral orifice of both sexes; the higher portions of the mucosa of the urogenital apparatus, male as well as female, seem to remain, as a rule, free from the eruption.

In general, the mucous membrane pocks, even where they are most abundant (in the mouth and throat), are more sparsely and thinly distributed than the skin pocks; but there are exceptions, as, for instance, the mucous membrane of the throat, which, of all the mucous membranes, is the favorite seat of the exanthem. Here, beginning at the anterior arches of the palate, on the tonsils, the uvula, the posterior wall, as well as (with the help of the nasopharyngeal speculum) in the vault of the pharynx, we see in variola vera, and still more in variola confluens, quite numerous and closely crowded masses of characteristic smallpox exanthem. Finally, this much is gathered from the numerous careful observations of the occurrence and localization of the pocks on mucous membranes in variola; that, leaving out of account the conjunctiva bulbi and the upper surface of the tongue, eruptions on the mucous membranes of the upper and lower passages are proportionately more frequent and more abundant when these regions are more exposed to the air, or especially when they are air-passages.

The development of the mucous membrane pock is quite analogous to that of the skin pocks; in other particulars, however, they are somewhat different. On account of the more delicate and more destructible character of the epithelium of the mucosa as compared with that of the skin, a superficial defect (erosion) is usually quickly formed in the pocks on the mucosa, so that it more rarely than in the skin penetrates deeply. Besides, the variola eruption on the mucous membranes is regularly introduced and accompanied by a diffuse catarrh of these membranes. In the mouth and throat, where we can best see these pocks and follow their development, the mucosa pocks appear as sharply circumscribed, small, millet-seed-sized macules, which are clearly distinguished from the diffusely affected mucous membrane by their brighter red color. These macules soon become prominent and change into papules. Vesicles often begin to develop on the surface of these papules, which therefore present a whitish, glistening appearance. But generally the thin epithelial covering of the vesicle is quickly brushed off, and an erosion then appears on the flat, papular elevation, surrounded by a fine whitish border (epithelial residue), from which later, by the destruction

of the papule, a small, circumscribed ulcer may develop. Where several such efflorescences stand close together, larger, irregular, and deeper ulcers may develop under certain circumstances, especially on the tonsils, but also in the larynx and other places.

The processes described on the mucous membranes are accompanied by certain annoyances to the patient which depend partly on the efflorescence and partly on the accompanying catarrh. Unpleasant burning sensations in the mouth and throat, in the nose and larynx, similar to, but more severe than, the corresponding sensations in the skin, betray the outbreak of the papules in the parts named, while increased secretion of mucus and saliva, slight dysphagia, and frequently hoarseness occur as symptoms of the accompanying diffuse catarrh. If the above-mentioned erosions and ulcers form, which usually occurs toward the end of the period of full development of the skin exanthem (at the end, namely, of the first week of the disease), these changes naturally cause more or less severe pain, especially in speaking and swallowing. All these symptoms of the disease are increased in the further course of events (see Period of Suppuration), but are present to a considerable degree even at this time, while the skin exanthem causes relatively little annoyance to the patient. This different behavior is explained when we consider, besides the early development of catarrh in the affected mucosæ, the greater rapidity with which, in comparison with the skin pocks, the mucosa pocks pass through their different metamorphoses.

Other Symptoms.—It may be considered as a characteristic peculiarity of regular smallpox, which most certainly distinguishes it from other exanthematous affections (measles, scarlet fever, spotted fever), that the eruption of the typical exanthem at the close of the initial stage is accompanied by a considerable remission of the pathologic symptoms then present, especially of the fever. This remission and improvement in the general condition is very remarkable, and occurs even in cases of the fully developed disease (or variola vera). Of course, in these cases the improvement is only transitory, and, with the beginning of suppuration, soon gives place to symptoms of renewed intensity.

Not infrequently the improvement begins just at the end of the initial stage, and before the first traces of the smallpox exanthem appear on the skin ; but in all cases it begins, at latest, with the appearance of the eruption. The pain in the head, as well as the typical lumbar pain, and all other troubles and pains of the first days of the disease, diminish at this time. If delirium is present or if the patient lies in a deep stupor, these symptoms of the initial toxemia likewise decrease, and gradually give place to a natural condition of the sensorium. Soon the

elevated body-temperature begins to fall and the pulse to become corre- spondingly slower. Thus, in all realms of the disease a very decided retrogression of the symptoms takes place on the appearance of the exanthem.

This retrogression now runs parallel in time with the advancing development and extension of the smallpox exanthem on the skin, so that, especially in cases of variola vera, corresponding to the slow pro- gress of the eruption from above downward, the restoration of a feeling of well-being and the decline of the fever are gradual. The tempera- ture, therefore, in the regular form of smallpox, generally falls toward normal, not quickly and suddenly, but rather after a protracted and often step-like fashion (with interpolated evening subelevations), ex- tending over from two to three days. When the eruption is com- plete,—that is, on the sixth day of the dis- ease,—the tempera- ture, even in variola vera, has almost or even entirely reached the normal, and there it remains for one or two days, even in the evening. Usually with the eighth day it begins to rise again, as this is the time of

Day of the Disease.

Fig. 1.—Variola vera. Three-year-old girl, not vaccinated. First week of the disease (initial stage, eruption complete, and beginning suppuration).

the beginning of suppuration. The peculiar course of the fever in variola vera in the first weeks of the disease (initial stage and period of eruption and full development) is illustrated in the following tem- perature curves (Figs. 1 and 2). The measurements were taken in the axilla.

The general condition of the patient, at the time of the apyrexial interval, has likewise become nearly normal. The sensorium is free, the patient sleeps quietly at night, the pains in the head and loins have completely stopped, and even the appetite is, in many cases, quite natural.

The complaints are now limited to some feeling of tension in the

, pock-covered skin and to the symptoms arising from the upper mucous membranes above described. No wonder, then, that this feeling of relative well-being toward the end of the first week of the disease awakens in many patients the hope that they will soon recover. But unfortunately it is not so in this disease; rather, after a brief pause of the disease, the period of real danger begins with the setting-in of the stage of suppuration, a time which holds in store for the patient, if not death, at least repeatedly renewed and often very distressing troubles.

Period of Suppuration.—The period of suppuration (or of maturation) begins, as a rule, in a variola vera with the beginning of the second week (on the eighth day), for at this time the previously clear contents of the pocks begin to become distinctly cloudy.

FIG. 2.—Variola vera. Forty-year-old man, vaccinated in childhood. First week of the disease (initial stage, eruption complete, and beginning suppuration).

Sometimes this change begins somewhat earlier (on the seventh day), but rarely later. With this a purulent change of the lymph is connected, in a greater or smaller number of pocks—a purulent infiltration of the pock-base, which may, and frequently does, lead to a softening of the superficial layers of the corium; also a considerable and extensive inflammatory congestion of the skin in the neighborhood of the pustule. Hand in hand with these congestive changes in the skin, and analogous to them, go an increase and further extension of the catarrhal disorders of the mucous membranes, which may pass considerably beyond the limits of the distribution of the exanthem. Furthermore, the rash, on account of deeper infiltration, may take on a more destructive character in different places to a very varied extent. Finally, depending on these local phenomena, renewed fever (suppuration fever) occurs, and also signs of a general disturbance of health appear. This general disturbance, provoked secondarily by the suppuration, is in many cases so severe that it causes death; for the fatal termination in variola vera is most frequently brought about by this cause, and takes place in this period of the dis-

ease. At other times death comes later, and is then a consequence of severe localization elsewhere, beginning in the period of suppuration and subsequently developing further (complicated smallpox). In this ulterior localization of the disease purulent processes generally play a prominent part. They are, like the suppurative process in the skin exanthem, to be regarded as the expression of a pyemic infection added to the specific variolous infection.

We are perfectly justified in regarding the period of suppuration in variola vera as a pyemic period of the disease, since it has been shown bacteriologically that the ordinary pus cocci (staphylococci or streptococci) are present in large numbers in the purulent efflorescences of the smallpox patient. (Compare Etiology, Parasitology of the Smallpox Virus.) The same pyogenic micro-organisms are found also in the blood and in many other local collections, just as in complicated smallpox. Pus in reality in each case of variola vera depends on a mixed infection, and the regular form of smallpox is, etiologically considered, not a simple, but a very complicated affection. According to clinical usage, only those cases of smallpox are classed as complicated in which the (mixed) infection is localized, not only in the skin and mucous membranes, but also in other places (compare above).

The duration of the period of suppuration is extremely variable ; it is, in general, directly proportional to the intensity and extension of the purulent process, and may thus be much prolonged by internal localization (as in complicated cases). If we are considering only the regular processes in the skin and mucous membranes (thus, a pure case of variola vera), then it lasts, on an average, less than a week (about five days), and the maximum of intensity then usually occurs in the middle of that time. The latter observation applies to the local symptoms as well as to the fever and other general disturbances.

In the skin the following changes may be observed in the pocks and their surroundings at this time. In the order in which the pocks appeared and came to maturity, they have assumed an increasingly opaque appearance and soon show a decided yellow color. On pricking such a changed pock, clear lymph no longer exudes, but a cloudy fluid—relatively thick pus ; at times, the individual pocks, as the suppurative change goes on, become more prominent, exhibit a smooth, hemispheric surface, and lose their central navel-like depression, if they possessed one during the stage of full development or maturation. But, with unpleasant sensations of pulsating and tension, an intense redness and swelling of the skin (areola or halo of the pock) develop around the individual pustules, by which the pocks are elevated and become extremely painful on the slightest pressure. These last-described changes in the neighborhood of the pocks also appear, as a rule, first on

the face and head, and later on the rest of the body (trunk and extremities), in obedience to the general law which governs the development of the exanthem in all its phases in variola vera. As the pocks in variola vera are very close together on the face and head, it is clear that here a diffuse and severe inflammatory edema may very easily and almost as a rule result from the mingling of the areolæ, causing such a change in the patient's features that he is almost unrecognizable.

The coalescence of the areolæ just mentioned in the variola vera discreta, which is quite usual in this form of the disease, may not be at all related to the coalescence of the purulent masses which forms the clinical and anatomopathologic criterium of variola confluens (see later).

The inflammatory edema often reaches a very severe and even excessive degree in those regions of the face and head on which the skin is loosely adherent or where a denser texture is wanting, especially on the eyelids, but also on the cheeks, the lips, the wings of the nose, and the lobes of the ear. The patient is, as can well be understood, much hindered and troubled by this ; thus, the impossibility of raising the lids or of using the eyes, the difficulty of nasal respiration, which compels the patient to breathe only by the mouth, the impediment to lip-articulation, and also the inability to close the mouth in the act of drinking, all add to his general discomfort. The inflammatory swelling of the skin in the more tightly fitting and more closely adherent skin of the head is not so marked, although even here the individual pocks are generally close together, just as in the cartilaginous portion of the concha auris and in the adjoining region of the external ear. But the sensitiveness and pain on pressure are here especially great, and are often so severe that mere pressure of the head on the pillow is sufficient to cause the patient the greatest torture.

On the trunk and extremities the pocks are generally sparsely distributed. Therefore confluence of the inflammatory areas is far less frequent here, and usually occurs only in certain regions. Nevertheless the local inconveniences are very severe, especially on the back and other parts on which the patient must lie. They reach their full development in these regions, as already indicated, somewhat later than in the head region, but latest of all, and also most severely, in the hands and feet, where suppuration sets in at last with all its accompaniments.

The number of pocks is usually quite large in these parts ; they are also influenced by the marked innervation of these parts, so that, especially in the fingers and toes, but also in the palms of the hands and soles of the feet, considerable disturbance of function and almost unendurable pain arise for the unfortunate patient.

The external picture presented by the individual pocks, especially on the palms of the hands and soles of the feet, in the stage of suppuration also, differs from that in other parts of the body (see above). In contrast to the condition elsewhere, the pocks are not much elevated above the level of the surrounding skin ; also a high degree of diffuse swelling is lacking in the volar and plantar skin. However, the beginning of the pustular metamorphosis of the pock, in these regions as elsewhere, is indicated by the opaque appearance and yellowish color, as well as by the intense and extensive injection of the surrounding tissues.

Many of the pocks on the face burst spontaneously at the height of suppuration from the pressure of their contents, and discharge the purulent mass, which dries to a thick yellowish crust covering the part. Other pocks have their tops rubbed off by pressure, especially on the back of the head, the back, and the buttocks. The pus discharged in quantities naturally soaks into and repeatedly saturates the bed-linen and the clothing of the patient, and soon, on account of the unavoidable decomposition, emits a very penetrating odor, which not only clings to the effects of the patient, but also taints the whole atmosphere of the sick-room. Finally, from the constant contamination of the skin with pus, the patient is in immediate danger of acute bedsores, which, in severe cases of variola vera, can often not be avoided in spite of the most anxious attention to cleanliness.

If the processes in the skin which have been described are by themselves quite sufficient to make the period of suppuration distressing to the patient, then the torture of the condition is considerably increased by the aggravation of all the symptoms in the mucous membranes. This aggravation of symptoms, caused by the advancing suppuration of the pocks in the mucous membranes, as well as by the increasing intensity of the accompanying inflammatory phenomena, asserts itself in all regions where the mucosæ are affected, and also far beyond those regions. Through these conditions, extremely painful, as well as often extremely dangerous, situations arise for the patient, and especially in yet other cases through complications which may outlast the smallpox process itself. As concerns the upper regions of the mucous membranes, which are the ones most frequently attacked, we find intense reddening with considerable swelling, hypersecretion, and hyperesthesia wherever we are able to examine directly ; for example, on the conjunctivæ, on the nasal mucous membrane, in the mouth, and in the throat. Greasy crusts of conjunctival secretion glue together the eyelids, already crippled by the palpebral edema, and make it entirely impossible to see. Nasal breathing becomes extremely difficult on account of obstruction in the nasal

fossæ—a condition which, especially in nurslings and young children, may prove fatal. The mucous membrane of the mouth is diffusely painful ; the salivary secretion is considerably increased and the secreted saliva, mingled with mucus, runs continually in viscous masses from the disfigured orifice of the mouth, which moves with difficulty, and is incompetent. The thick and ill-shaped tongue can make only stammering sounds and, even by its volume, limits the space needed for the vicarious mouth-breathing. At times, but fortunately rarely, deep-lying abscesses are formed in it (glossitis variolosa). In such cases volume of the organ is greatly increased, its motility is almost completely suspended, and, by pressure on the epiglottis, death from suffocation may follow in a very short time. Very severe, and very alarming also, are the anginal symptoms arising from the pharynx ; this is especially true, of course, when the inflammation does not remain superficial, but, at the time of the suppuration of the throat pocks, goes on to the formation of tonsillar abscesses or to some other phlegmonous processes in this region (for example, retropharyngeal abscesses). Furthermore, the mucous membrane of the Eustachian tube, and often also that of the middle ear, however little they may be directly occupied by the exanthem (see above), are the seats of a severe catarrh, which causes unpleasant sensations in the ear, tinnitus, and temporary deafness. Retention of the secretion in the tympanic cavity soon leads to penetration of the tympanic membrane and to subsequent otorrhea.

In these phenomena the first cause for the other severe ear difficulties (see Complications and Sequelæ) can be found. The voice, because of the participation of the larynx, is generally hoarse, and may be entirely lost ; many patients are also annoyed by a continuous irritating cough, from the same cause. Very dangerous suffocative conditions arise in children from the diffuse swelling of the respiratory mucous membranes ; but also in adults a very threatening difficulty in breathing may arise when the swelling of the aryepiglottidean folds increases to edema of the glottis, or when the suppuration of the laryngeal pocks, penetrating deeply, causes a perichondritis laryngea.

Less noticeable, because, as a rule, less marked, is the part taken by the mucous membranes of the lower portions of the body ; but even here corresponding symptoms of the disease in variola vera are not wholly lacking during the further course of the period of suppuration. The following are the most frequent complaints and symptoms : unpleasant, burning sensations in the anus with mucopurulent discharge and, especially, difficult and painful defecation; analogous subjective and objective symptoms in the region of the vulva and vagina in women ;

finally, some dysuria. Less frequent, and rather to be considered as complications, are periproctitic abscesses, suppuration of Bartholini's glands, and other similar occurrences.

The pathologic picture of variola vera in the period of suppuration is finally completed by the renewal of the intense general toxemic symptoms. As a rule, with the setting-in of suppuration in the skin pocks, the temperature, which had been normal during the apyrexial interval of the disease, begins to rise, and at the same time, with the renewal of the fever, the pulse-rate and frequency of respiration increase. The type of the fever curve during the period of suppuration (or the suppurative fever of smallpox) is somewhat variable, and is often determined by accidental conditions. The most frequent form, especially in uncomplicated cases of the disease, is a remittent fever, which rises gradually for a certain number of days, and, after reaching its maximum, falls gradually in a similar way.

The suppurative fever of variola, in the formation of a curve, shows an essentially different character from that of the initial fever of the disease. A sudden rise of temperature in particular is usually lacking. This fact shows that the cause of this second fever is not the same as that of the first, which, under all circumstances, must be regarded as the direct product of the specific infection of variola. All authors up to this time have supported the view expressed by me that this second fever of variola vera depends etiologically on the suppuration, and for this reason must be considered as a suppurative fever.

L. Pfeiffer* now looks at this question from another standpoint. He regards the second fever of variola vera also as due to the specific variolous infection, at least at its onset. He supports his theory by the views of Van der Loeff that the specific parasite (Cytorrhyctes variolæ) is said to circulate again in the blood at the beginning of the renewed febrile stage as the young form, proliferated from the skin exanthem. For the further course of the suppurative fever, Pfeiffer, on the ground of bacteriologic findings in the pock-pus, admits the influence of the pyogenic cocci (staphylococci and streptococci). It will be the task of further investigations and observations to test fully the correctness of these statements of Van der Loeff. Another ground for regarding the renewal of the elevation of temperature about the end of the first week as due to a specific variolous infection is, according to L. Pfeiffer, that the temperature is said to rise, as a rule, in the vesicular stage of the efflorescence before the pock lymph begins to be turbid. This statement is in direct contradiction to the observations made by all other authors, including myself. It may rather, according to all previous experience, be regarded as true that a noticeable second elevation of temperature occurs only and develops gradually when the pocks on the head and face appear markedly pustular and the inflammatory edema begins in the regions surrounding.

* *Loc. cit.*

The usual behavior of a suppurative fever in variola vera is indicated by the following temperature curves, which represent the direct continuation of those found on pages 55 and 56 (Figs. 1 and 2), and are taken from the same cases.
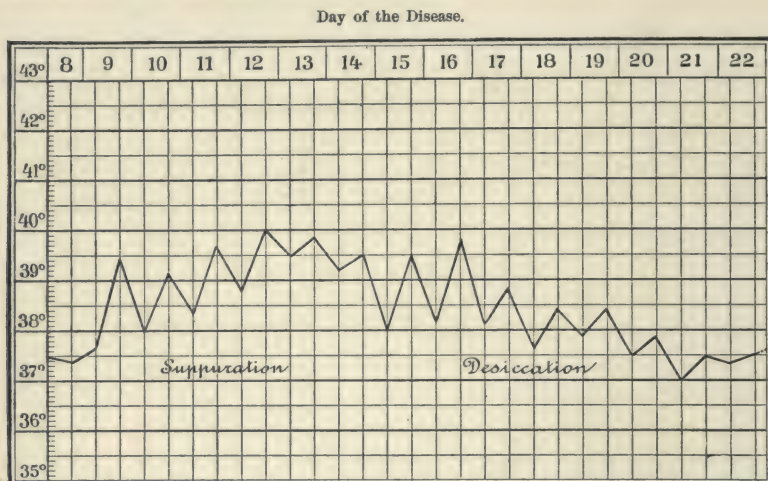
Day of the Disease.

FIG. 3.—Variola vera. Three-year-old girl (not vaccinated; compare Fig. 1 on page 55). Suppurative fever and desiccation (second and third weeks of the disease).
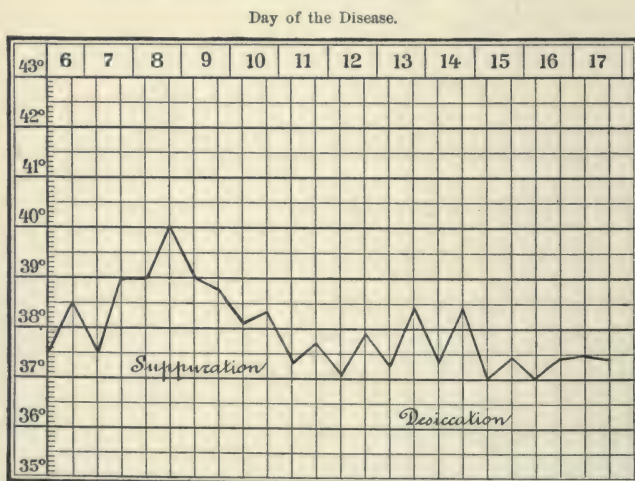
Day of the Disease.

FIG. 4.—Variola vera. Forty-year-old man, vaccinated only in childhood (compare Fig. 2 on page 56). Fever of suppuration and desiccation (second and third weeks of the disease).

The maximum of temperature during the suppurative fever only rarely, in cases pursuing a favorable course, reaches the maximal temperature of the initial fever. If, on the other hand,—as unfortunately

happens not infrequently,—death ensues during the suppurative stage, then unusual conditions of the temperature curve may be observed during the last hours of life ; among these are the so-called hyperthermia or hyperpyrexia, and more rarely, on the other hand, antemortem depression of temperature, and even collapse of temperature. (For more minute details of hyperthermia, see under Variola Confluens in a later part of this work.)

Among the other symptoms of purulent blood-poisoning may be mentioned the cerebral irritability which occurs with remarkable frequency at this time and often reaches a very considerable degree. This depends in part on the tortures which the poor patient has to suffer, and in part

Day of the Disease.

	2	3	4	5	6	7	8	9	10	11

(43° … 35° temperature scale; labels: Initial stage, Eruption, Full development, Suppuration; † marked near 42° on day 11)
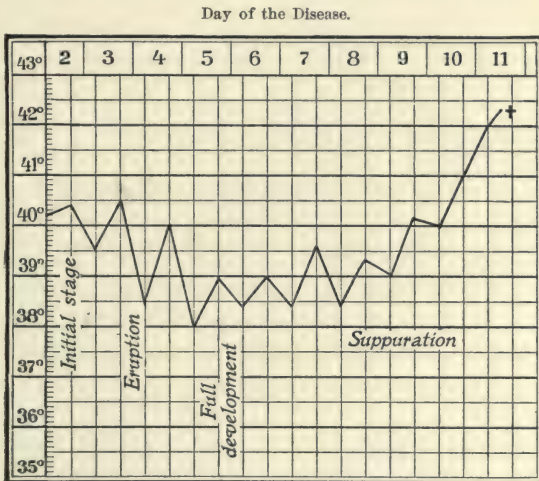
FIG. 5.—Variola vera gravis. Death on the eleventh day, the temperature being hyperpyretic (43-year-old man vaccinated only in childhood).

on an immediate toxic influence on the brain through the toxic properties of the pyogenic cocci. Besides the great psychic distress and the jactitation, there is often delirium, which occurs very frequently, not only in inebriates or in nervous patients, but also in less susceptible individuals ; this delirium is generally of a very excitable type. Great danger often arises, for both the patient and his surroundings, if he, as is often observed, indulges in unexpected violent actions, and traumatic consequences may follow.

More than once, unfortunately, have I seen smallpox patients in the delirium of the purulent stage, in spite of the impeded motility of the muscular system and the great painfulness of voluntary motion, spring suddenly from the bed, destroy the surrounding objects, or spring from the window inflicting severe injury on themselves. Therefore the patients

need close watching in this stage; even more so than in the initial stage, in order that they may not injure themselves or others.

But acute exhaustion may also be the consequence of this severe condition of irritation, for not infrequently sudden death occurs in the midst of such an exciting scene, due probably to heart paralysis. More frequently death during suppuration is due to a gradual weakening of the vital functions. Increasing stupor, with small, very frequent, and finally intermittent pulse, stertorous, irregular breathing, and beginning tracheal râles, announces with some certainty in such cases, as in other severe toxemias, the coming catastrophe. That certain occurrences in the upper air-passages might cause death by suffocation was expressly mentioned in the consideration of the symptoms in the mucous membranes.

In cases of variola vera which run a favorable course, on the other hand, if no other complications intervene, the highest point is usually reached in the middle of the second week, and is then passed. The improvement begins, not quickly, but gradually, and the same is true for the local as for the general symptoms. This indicates that a sharp time-limit cannot be set between the period just described and the following period of the disease.

Period of Involution (Desiccation and Decrustation).—The involution of the smallpox exanthem is accomplished in variola vera amid gradual abatement of the inflammatory congestion in the neighborhood of the pocks. By this means, *eo ipso*, the suppurative process is more and more strictly localized. As this occurs, the purulent contents dry from within and also a drying (desiccation) of the purulent deposit on the surface takes place, which is in this way prepared for its being pushed off later on (decrustation). By this last-named process the surface of the skin is entirely freed, and the local process seems then really ended. Of course, traces of the exanthem remain behind always and everywhere, which, according as the lesions were in places more or less intense, either remain permanently (as smallpox scars) or completely disappear in time. This is in general the course of events; in individual cases the following peculiarities may be noted: The same rule is followed here as in other stages, and the involution of the smallpox exanthem does not take place on all parts of the body at the same time. It follows rather the scheme and order of events which have been noted for the eruption, the development, and the suppuration (or maturation) of the eruption—taking place first on the face and the head; next, descending, on the trunk; and last of all, on the extremities. So it happens that on the hands and feet the suppuration is in full course at

the time when, on the face and head, desiccation has quite unmistakably taken place. Far more rarely we may observe in variola vera a premature retrogression of the phenomena in the parts later attacked, so that the desiccation and also the decrustation begin more nearly simultaneously over the whole body. When this occurs, as it does now and then in individual cases, the duration of the period of involution, which otherwise is usually long (two weeks and over), is correspondingly shortened.

In certain regions we recognize the retrogression first by the abatement of the inflammatory edema, the diminution of the diffuse redness and swelling, and the disappearance of the areola. With this, the features of the patient, which up to this time have been extremely disfigured, regain more and more their normal outlines; the same may be said of other parts of the body which have been especially affected (as the hands and feet). At times the appearance and condition of the pus scabs and of the still uninjured pocks over the skin change. First, in consequence of drying, they lose their honey-like color and their greasy softness, become brownish, hard, and brittle, and continuously shrink more and more toward their base, to which they in a short time become adherent. Later on the pustules which remain intact soon become of a distinct brownish color, lose in so doing their hemispheric outline as well as their smooth surface, and shrink finally to hard, dark brown, and generally somewhat rough, ill-shaped forms. As such they, as a rule, cling firmly to the skin somewhat longer than the scabs already described before they are cast off (compare later).

With the cessation of the inflammation the local inflammatory pain in the skin (caused by pressure, etc.) also ceases, in most cases quickly. During desiccation a very unwelcome addition to the recovery is that of an unendurable itching in the affected parts, inviting scratching, which, by causing new injury, may easily interrupt the regular involution of the exanthem. The condition of the patient becomes more and more endurable, as, with the abatement of the edema, the eyes can be opened again, the nose performs its functions in some measure, the lips can be used, and the rest of the body can be moved without the severe pains which have been so distressing. The relative well-being of the patient is markedly increased by a considerable abatement of the painful symptoms connected with the mucous membrane, and finally a cessation of the fever and of the general disturbances takes place.

As in the region of the cutis, the improvement makes successive advances; the buccal, nasal, and pharyngeal phenomena of inflammation disappear, and likewise all other expressions of the variolous affection

of the mucous membranes (in the larynx, in the auditory apparatus, in the lower regions of the body, etc.). Indeed, the restoration to health in these affected mucous membranes, at least in normal and uncomplicated cases, takes place usually somewhat more quickly and more completely than in the skin, as the conditions connected with them are mostly favorable, and especially as the variolous process has been less destructive in its influence.

The fever, which stood highest at the time of the maximal distribution and intensity of the suppuration, abates with the abatement of the same and with the beginning of desiccation. The fall of temperature is generally, as already mentioned, gradual, and toward the end of the second week the normal temperature has usually been reached. If this happens during the progress of the desiccation of the skin exanthem, a supplementary elevation of temperature to fever height does not usually again occur if complications neither develop nor still exist which might have a fever-producing influence. There is no special "desiccation fever," such as is mentioned now and then in writings on smallpox, and which is said to be due to the desiccation itself. With the cessation of the fever of suppuration which accompanied the pus formation, the delirium and other symptoms of the general toxemia disappear, usually *pari passu* with the fall of temperature. The sleep and appetite return; the bowels, which have hitherto been almost always constipated, become regular; the urine, which has been of high specific gravity and full of sediment, becomes gradually clear and abundant; and the whole man, though still very weak and much exhausted by the past storm, nevertheless regains from day to day strength and health.

But the exuviæ must still be cast off, a process (decrustation) which lasts a variable time, and, in severe cases of variola vera, frequently a very long time. While the dried pocks cling longest to the palms of the hands and soles of the feet on account of the thickness of the epidermis,—where they are often found, after three weeks and more, as hard, lentil-shaped forms in the horny layer, and may be shelled out of their epidermal husk,—yet, over and above these, pock scars may remain behind wherever there were deeper lesions of the corium. In these places the dried pock with its lower surface sinks into the supposed defect of the thick skin and forms not so much an accumulation as a lodgment in this, which naturally delays the decrustation.

As the number of these deeply penetrating masses of pus in variola vera (especially on the face and head) is frequently quite large, the whole process of decrustation requires a correspondingly longer time. Finally, if such a deeply seated pock scab is removed too early by

scratching, then one sees, in the place formerly occupied by it, a still unhealed defect of the corium, on which a new crust has to form before healing can take place. It is clear that by such imprudent manipulation the time of the local recovery is still more delayed.

Pigmentations of the skin almost invariably remain behind after decrustation as immediate results; these have at first a distinctly hyperemic color, and are for a certain time correspondingly sensitive to the influences of the external temperature. Later on, they lose this character and become brownish in color, then gradually pale, and after some months entirely disappear. These pigmentations, during their continuance, give to the smallpox convalescent a peculiar spotted appearance, which is especially marked in the face, but, as already noted, is not of long duration. Many of these pigmented spots form at first flat elevations (papules), this peculiarity being due generally to a remnant of the hyperemic swelling of the papillæ; these soon become level again, and, like the pigmentations, leave no permanent trace. Other pigmented areas lie at the level of the rest of the skin, hence are purely macular and usually leave no permanent mark. Still others correspond to shallow depressions of the skin, which are related to a pressure atrophy of the papillæ in these places. This simple atrophy of the papillæ, caused by too long continuance of pressure from the purulent exudate resting upon them, is not capable of restoration; yet the stigmata resulting from it, although permanent, are not especially disfiguring, and should be distinguished from the true smallpox scars. Finally, there are areas which are pigmented at first, but which become the permanent smallpox scars; these, therefore, are likewise at first hyperemic and dark-colored, but later assume a whitish color.

While the surface of the body of the smallpox patient is becoming completely freed from the remains of the exanthem, and while the residual changes of the skin just described are developing, the general convalescence in uncomplicated cases of variola vera is in most instances making rapid headway. The whilom patient, after the miseries endured during the preceding weeks, experiences the increasingly pleasant sensations of happy recovery from severe illness, eats with avidity, increases rapidly in weight, thus replacing what he had lost, and finally tries to employ himself suitably again, physically as well as mentally. In the former, he usually succeeds more quickly than in the latter. The hair of the head and beard and other places falls subsequently, and thus for a time reminds him of the horrors he has passed through; but later there is complete restoration, if the hair-bulb has not undergone a destructive process.

The permanent smallpox scars, the number of which in variola vera is generally not very great, and which usually remain on the face, the scalp, and the hands and feet, correspond to all those places in which the pustular exanthem, by a purulent softening of the papillæ, causes their destruction. This defect, like other similar conditions, is repaired by formation of loose, vascular, definitive scar tissue. According to the intensity of the granulation process, and according to whether the spot is just freed from the pock crust covering it, it appears slightly elevated, level with the surface, or even distinctly depressed. The last condition is probably true in the majority of cases. In the further course, and as an expression of the subsequent retraction of the newly formed connective tissue, the flat and also the elevated granulation masses usually change into distinctly depressed scars. These latter then remain for the rest of the patient's life as disfiguring reminders of the disease he has undergone, and by their great number give to the countenance a very characteristic appearance. The individual pock scars after variola vera discreta are of about the size of a lentil, of radiate structure and whitish color, while in time the pigment, which is present at first, is entirely lost.

This really completes the description of an ordinary variola vera (together with its results); and the principal form of the disease, the true and regular variola, is somewhat fixed clinically in its essential symptoms. Besides this chief type,—which may be so called because, in the greater epidemics of smallpox and in the undiminished (natural) predisposition to the disease, a relatively greater percentage of all cases nearly corresponds to it,—for the rest of the cases different side-types can be found, a short description of which I will attempt in the following pages. In the description and naming of these different varieties of variola it must be understood that all cases of variola have without exception one etiologic origin, and that clinically, also, the special varieties of the disease are in manifold ways, by intervening classes and transition forms, related to each other.

The more important general modifications of smallpox are, on the one hand, those which show an increased intensity and also malignancy of the disease : malignant smallpox ; and, on the other hand, those in which the opposite is true : benign forms of smallpox—a classification and distinction the practical value of which is at once apparent. To the former belong the cases of variola confluens and the hemorrhagic forms of smallpox ; to the latter, on the other hand, varioloid (variolois) and variola sine exanthemate.

Variola Confluens.—By " variola confluens," or, in German,

"zusammen fliessende Pocken," we understand cases of variola with special development of the typical skin exanthem, so that, during the suppurative, process, the purulent masses, which are at first discrete and represented by single pocks, in certain regions, and sometimes for a considerable distance, fuse with each other (flow together). The condition necessary to the local fusion of the suppurative pocks is, naturally, that the individual pocks, during the period of eruption and maturation, shall stand so close together *in loco* that their boundaries shall touch and crowd each other. But this circumstance alone does not necessarily imply the subsequent true confluence, for even the pocks which stand closest together still retain, during this earlier period of the disease, their character as single individuals. Just as little is it required that, under such conditions, a confluence of the purulent masses should later (that is, during the suppurative period) necessarily take place; for these masses often remain discrete until they dry, as is taught by experience and is *à priori* obvious. What is really essential for local confluence of the pocks during suppuration, and for the occurrence of variola confluens in the anatomoclinical sense, is, with the sufficiently close grouping of the exanthem, such a vehemence of the suppurative process that the tissue boundaries between the individual pocks may in many places become liquefied and be mechanically broken through. By this the malignancy of the local process is characterized, as also, on the other hand, the malignancy of the corresponding clinical form of smallpox.

Even in the severest cases of this kind the confluence never involves the whole body, for the condition of the exanthem is never so crowded all over the body as to even approximately fulfil the above-mentioned essential condition. The confluence during suppuration is observed most frequently and most extensively on the head and face, and also on the hands and feet; in other words, in those regions where the local variolous process is most severe. In especially severe cases small parts of the back and other parts of the extremities may also be involved, but this is by no means the rule. It is surprising that in those regions where previous mechanical or chemical irritation had occurred, and on which in consequence (compare the earlier note on this point) a specially thick early development of the exanthem, limited in extent, took place, true confluence during suppuration is rarely observed. Hence it is that these conditions do not involve that bad prognosis which is justly attributed to confluent smallpox.

Variola confluens was, in prevaccination times, not only absolutely, but also relatively, far more frequent than now under the régime of protective vaccination, for it regularly formed a more or less considerable

contingent of the cases in the far more frequent and more extensive variola epidemics. In still greater measure, on account of its malignancy, it contributed to the general mortality from smallpox. At present, these worst forms of the disease are met with in the non-vaccinated (children as well as adults) and in those who have been vaccinated only once (in childhood) and who are attacked by the disease in advanced life, when the protection from inoculation is entirely exhausted; otherwise, and under more favorable personal conditions (for instance, in the presence of successful revaccination), variola confluens is almost unknown.

Personal predisposition appears to have played the chief rôle in former times in the causation of variola confluens, as neither an influence of the *genius epidemicus* nor any *propagatio per continuum* (from case to case) for this modification of smallpox can be found in the reports of the epidemics of early times. On what this special personal predisposition to variola confluens rested, is unknown.

No marked difference between confluent and non-confluent smallpox is noted regarding the duration of the time of incubation; somewhat more positive statements may, however, be made concerning the initial stage. This is scarcely ever mild in its course, and, almost without exception, is accompanied by very severe symptoms. High fever, intense pain in the head and in the lumbar region, the typhoid or ataxic state, and marked gastric symptoms (especially continuous retching and vomiting) are present with great constancy. Although, according to what has been said above, in cases of simple variola vera discreta, and even in not a few cases of varioloid, such a condition may be present, yet it is the rule in variola confluens, so that there are almost no exceptions. Still more noteworthy is it that the outbreak of the exanthem in variola confluens is quite frequently hastened so that it begins before the third febrile elevation (thus from twelve to eighteen hours too early). The eruption begins very frequently, if not regularly, at the end of the second day of the disease or at the beginning of the third. With still greater frequency the eruption spreads rapidly, so that the closely crowded exanthem, in the typical order of events, extends, very quickly from the head downward, over the whole body. Taken all in all, rarely more than two days more pass before the eruption has appeared on all accessible portions of the body. Through the peculiarity just described, the general pathologic process in variola confluens is characterized as a tumultuous one, even during this early period, a feature which becomes more prominent in the further course of events.

Unlike the course of the temperature in variola discreta, although there is a lowering of the temperature in the period of eruption, this

remission is usually not complete, and a temporary apyrexia does not usually occur during the so-called "intervening stage" ("Zwischen-periode"). Rather does the temperature, after the full development of the eruption, almost always remain above the normal, while it rises immediately, with the stormy introduction of suppuration, to fever height. Just as there is no complete abatement of the fever, so we do not see that interesting improvement in the general condition which, in variola vera, so strikingly separates the initial stage from the period of suppuration in time as well as in symptoms. Some clearing up of the sensorium and a little relief from the severe lumbar pains are usually all; in other cases, the Charybdis is followed almost immediately by the Scylla, to which, after a few days of the greatest suffering, the unfortunate patient generally falls a victim during the suppuration. In the development of the eruption in this form of smallpox, papule is elevated close beside papule over a considerable area on the head and face, and in this form also on other portions where confluence later occurs. From this a certain degree of diffuse swelling results, and also an increase of volume in the parts attacked. The individual papular elevations are, as a rule, somewhat smaller than in variola discreta, probably because they, singly, can get less space for their proper spread in width. If one stretches his hand over the affected skin at this time, he has the sensation of having felt a rough grater or embossed leather. In these numberless papules, which soon become very red, vesicles quickly develop, which rapidly increase in size and the contents of which quickly become turbid. At this stage, in many places, the hitherto discrete outlines of the individual pocks disappear, and, with further increase of suppuration, there are formed from the hordes of confluent pocks irregularly bordered, flat, large pustules, which, singly, are sufficient to take possession of different smaller parts of the face, of the head, of the back of the hand, etc. To complete the picture such numerous confluent masses, at first still distinct, unite through their close proximity into a single immense pustule, the diameter of which is equal to that of a plate or more, and which, for example, may cover almost the entire face of such a patient as with a homogeneous, whitish-yellow mask.

The severity of the accompanying inflammatory edema, which in no other form of smallpox reaches so high a degree as in the cases of variola confluens, corresponds to the vehemence and extent of the suppuration. The severity of the tense and throbbing pains, the sensitiveness of the skin to pressure, and the other similar subjective symptoms also correspond, so that the limit of endurance seems over and over

again to be all but reached. No wonder, therefore, that not infrequently the horrible tortures which arise in connection with the skin cause most violent emotional disturbances, and that actual frenzied conditions result. (See below for further particulars.) The condition of the patient at this time is rendered still worse through the intense participation of the mucous membranes in the process, for these also are unusually affected in confluent smallpox.

The localization of the pocks in the mucous membranes in these cases is approximately the same as in variola discreta, but the number of pocks in the upper passages is usually much greater, and the accompanying diffuse catarrh is highly developed both in intensity and in extent. The pocks frequently become confluent in the mucous membranes of different parts (of the mouth, nasal fossæ, throat, and finally also the larynx), and, by the fusion of the pustules, more extensive, irregularly shaped, and very painful ulcerations are usually soon formed in the mucosa. Much more frequently than in variola vera, one meets consecutive suppurative processes in the depths of the adjacent tissues— for example, acute glossitis apostematosa, tonsillar and retropharyngeal phlegmons, perichondritis laryngea, etc. By affections like those named above, but oftener by the occurrence of edema of the glottis, the lives of the patients are much endangered during this period, and they generally die from suffocation. At other times, these dangerous localizations outlast the proper critical point of the disease, or even develop somewhat later, and yet prove fatal to the patient. In variola confluens, purulent metastases and localization in distant internal organs frequently arise, and with them the risk that from such occurrences various ills and various dangers to life may sooner or later arise. In brief, then : The general condition of the patient, on account of all these local events and accidents, is or becomes extremely precarious in variola confluens from the beginning of suppuration. It becomes so without exception, and far more at this time on account of the intense and often quite alarming character of the accompanying symptoms which arise directly from the general infection.

The fever, which, as will be remembered, moderated during the development of the eruption only very imperfectly and transitorily, is immediately renewed with great violence on the occurrence of the suppuration. Temperatures of 40° C. and upward, with only slight thermic remissions, and correspondingly high pulse-rate, are the order of the day toward the end of the first week, and still more so in the second week of the disease in this form of smallpox. The more the fever increases with the suppuration, the more is the severe toxemia expressed

by all imaginable kinds of nervous symptoms, especially by delirium. A frenzied state, in which the patient strikes, screams, leaves his bed, runs about, etc., belongs to this stage. If now, as is unfortunately very frequently the case, death occurs at the height of the general disease through the intensity of the toxemic process, then, as a rule, the fatal issue closes the terminal phenomena by acute paralysis of the vital functions. The patient, who was formerly generally described as excited, becomes comatose, no longer responds to treatment, and tracheal râles are heard. The pulse becomes extremely frequent and scarcely perceptible, and, like the respiration, finally intermittent.

With relative frequency the already high febrile temperature, especially in variola con-

FIG. 6.—Variola confluens (according to Curschmann). Death with hyperpyrexia on the tenth day of the disease (fourteen-year-old girl).

fluens, is raised with constant rapidity to excessive heights (42° C. and over), and the *exitus letalis* accordingly follows in many cases, with the symptoms of the terminal or antemortem hyperpyrexia, already mentioned under variola discreta. (Compare p. 63.)

In this hyperpyrexial state, even where, as in variola, it develops from a febrile condition, we are concerned, in all probability, not simply with a maximal fever or one which has become maximal, but with something else, something new, essentially different from the fever and, in these cases, added to the fever. And we will not be far wrong if we regard this immoderate and ominous increase of temperature at the time of the death agony as a sign of sudden and complete cessation of the functions of the mechanism which regulates the temperature, due to a rapidly advancing paralysis of the nerve-centers regulating this mechanism.

In the rarer cases in which the patient afflicted with variola confluens survives the period of suppuration, the abatement of the local and general symptoms is generally considerably slower than in variola discreta. In the first place, the desiccation of the skin rash lasts a long time, because, under the large and coherent crusts in the region of con-

fluence, the suppurative process very obstinately persists. Very often it is observed that after the large crusts are loosened for the first time, new secondary crusts are repeatedly formed over the same areas, before the granulating cutaneous ulcers cease to suppurate, the granulation tissue changes to scar tissue, and thus the healing process becomes defini-
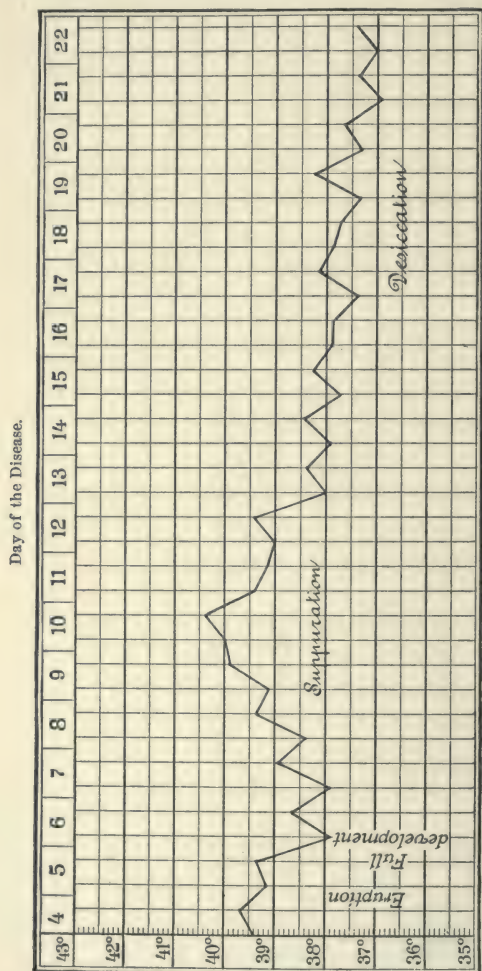
Fig. 7.—Variola confluens with healing process. Relatively mild case with relatively low suppurative fever. Confluence of the exanthem on forehead, nose, and backs of both hands (seventeen-year-old girl, never vaccinated).

tive. The changes in the mucous membranes also need a longer time for their adjustment, and the pathologic symptoms arising from them generally abate very slowly.

As the fever and the other toxemic symptoms genetically so closely depend on the suppurative process, it is easy to understand why they are

equally persistent, and why it usually takes so long to reestablish even tolerably good health. In this way it happens that the patients, even when no other localizations and complications exist which should have any pyretogenic influence, yet have fever until late in the third week or even longer; that the sensorium, enthralled by delirium, very slowly clears up; and that all other signs of the general perturbation pass very tardily into the background.

As regards the disfiguring marks which remain in the skin of the face and elsewhere after variola confluens, we have, thanks to the preventive influence of vaccination, rarely and exceptionally the opportunity of seeing them. As such smallpox patients are almost always those who have not been vacinnated or who have not been properly revaccinated, such specimens, from an esthetic standpoint, afford very impressive living warnings against the baneful phrases of the modern opponents of vaccination. Indeed, the permanent disfigurements which the destructive processes of confluent smallpox leave behind in the human countenance are often truly fearful. Where the confluence existed, we see not, as after variola discreta, small, round, isolated scar depressions, but, instead of these, extensive, irregular scar-formations, which are frequently crossed by firmer strands and, by the traction of these, are unequally distorted in different directions. These scars are most disfiguring when, occurring in the regions of the eyes or mouth, they are complicated with ectropion of the lids or lips. They have also, as can readily be understood, a lasting influence on the function of these parts. But elsewhere also in the face, these scars may, by their dense structure as well as by the formation of adhesions, hinder the free action of the corresponding muscles and exert a disturbing influence not only in the play of expression, but also in chewing and talking.

Hemorrhagic Forms of Variola.—Hemorrhagic smallpox (bloody smallpox or black smallpox) is generally characterized as a combination of variola with a hemorrhagic diathesis. This event may occur at different times, so that the hemorrhagic character of a case of smallpox may be manifest during the initial period, while in other cases it is shown first after the appearance of the exanthem. Accordingly we distinguish two forms: primarily hemorrhagic and secondarily hemorrhagic smallpox. The former is known as purpura variolosa; the latter, as variola pustulosa hæmorrhagica. Both forms surpass in malignancy all other forms of smallpox.

A closer insight into the genesis of hemorrhagic smallpox of both kinds is for the present impossible. This is partly due to our ignorance of the nature of the hemorrhagic diathesis, but partly also to the seemingly quite

anomalous union of the same with variola. A special malignancy of the smallpox virus is not the only reason, for, if it were, a propagation of the hemorrhagic smallpox case *per continuum* by infection would have been more frequently observed; hence this doubtless does not happen. That it concerns a mixed infection of variola with hospital gangrene, as L. Pfeiffer* assumes both for purpura variolosa and for variola pustulosa hæmorrha-gica, is likewise untenable, as hemorrhagic smallpox cases occur without any relation to hospital gangrene. Until further investigation, it remains undecided what the determining factors are and whether the same combinations of circumstances are concerned every time.

Purpura Variolosa.—Purpura variolosa, or primarily hemorrhagic smallpox, is, of all the known forms of smallpox, undoubtedly the worst, as it is always fatal in a few days. In symptomatology, too, it deserves special attention, because from the beginning it differs most of all the forms of smallpox from the regular type of the disease. This is indeed so far true that no one without an intimate knowledge of the circumstances, and especially without an acquaintance with the prevalent epidemic conditions, would enumerate the cases of purpura, on account of the clinical symptoms, under variola, so different from the normal does the picture of this disease appear in most of its relations. But that it is nevertheless smallpox is shown by the fact that purpura arises by infection from otherwise undoubted smallpox cases, as well as by the fact that it may give rise to ordinary cases of smallpox. Accordingly, it is undoubtedly variolous, however unsatisfactory in all else the knowledge of its special pathology may remain.

The occurrence of purpura variolosa shows great variations in frequency, for in many epidemics (among others, in the great pandemic of 1870–1872) it occurred relatively more frequently ; in others, relatively more rarely, or even was not observed at all. The so-called "*genius epidemicus*" is probably of some, but by no means of paramount, importance. For even in the most extensive smallpox epidemics, and especially in times of relative frequency of purpura cases, the latter still remain as isolated occurrences in the larger group of smallpox cases genetically related to each other without any tendency to the "*propaga-tio per continuum.*" From this it clearly follows that besides the "*genius epidemicus,*" yet other (accidental or individual) forces must be at work to cause that fatal combination of circumstances which brings about a case of purpura.

Very little is definitely known about these conditions. Age and sex seem to have some influence in so far as purpura favors the youthful and vigorous and that it is observed in females more frequently than in

*Loc. cit.

males.   Pregnancy especially and the puerperium seem to create a kind
of predisposition.   An exclusive relation is even said to exist, as if
purpura could not attack aged individuals, men, or non-pregnant women.

The prevalence of purpura among the young and vigorous is empha-
sized by later authors (Curschmann).   My own few observations assert
this relation only in so far that young adults are attacked almost exclu-
sively.

That alcoholism, evil habits of living, and other weakening forces
exert, as is asserted, an influence on the development of purpura vario-
losa is untrue, and such opinions are doubtless based on a mistake in
confounding the primarily hemorrhagic form of smallpox with variola
pustulosa hæmorrhagica.   (Compare later.)

On the other hand, it cannot be denied that vaccination and espe-
cially revaccination exert a relatively powerful protection against vari-
ola in general, and still more against both kinds of hemorrhagic variola
—at least, it is certainly one of the rarest of all occurrences to find after
repeated successful vaccinations, smallpox, if acquired, ever assuming
the hemorrhagic character.

The peculiar course of purpura variolosa is as follows : The stage of
incubation is frequently surprisingly shortened, and lasts, according to
Zuelzer, on an average only six to eight days, reminding one in this re-
spect of the shorter stage of incubation in scarlatina.   Prodromal symp-
toms (namely, some lumbar pain) occur more frequently at this time than
in the other types of smallpox.   The disease sets in with extremely vio-
lent general and local symptoms ; among the first, however, the febrile
symptoms are decidedly less prominent than other toxoneurotic symptoms.
An initial chill or an initial rigor is usual in purpura, and the tempera-
ture in this form of variola rises in the beginning to fever height.   At
the same time the high readings reached are relatively low in comparison
to others in the initial stage, scarcely reaching 40° C., and in most cases
remaining considerably lower.   But a very intense feeling of general
malaise as well as severe prostration exist from the beginning, and the
pulse is, from the first, correspondingly small and weak.   The sensorium
remains surprisingly free, and delirium is wanting, not only during the
rest of the course of the disease, but even up to death itself.   On the
other hand, severe pain in the head and lumbar pains of greater violence
than in any other form of smallpox are generally present.   To this are
added other painful sensations, as a high degree of precordial distress,
together with severe, closely related pains in the epigastrium.   Of other
symptoms, we find nearly continuous retching and vomiting, thus com-

pleting, on the whole, a pathologic picture which, in its chief features, reminds one very strongly of poisoning with acrid substances.

Usually on the second day of the disease, but under some circumstances even earlier, a dark scarlet-red flush begins to appear on the back and extremities, and in less degree on the face. Within the diffuse erythema are found very numerous small macules (varying from a pinhead to a lentil in size), and, mingled with these, a variable number of larger, irregular macules of purple color, the color of which does not disappear on pressure, and hence is of hemorrhagic origin. In the face the single, larger extravasations (ecchymoses) are usually prevalent. They are found here in different places, particularly in the neighborhood of the eyes, and in the region last named are complicated with sanguinolent edema of the lids and conjunctivæ. The scalp not infrequently remains free from hemorrhages ; they are much more numerous on the back and extremities, and here all sizes are observed. Thus, within a short time a very characteristic picture of the disease is presented on the surface of the body, a dark color-mixture of flaming red and purple, which imprints on such cases in advance the stamp of ill omen and disfigures the features of the patient in a very dismal way.

While these changes are taking place in the skin, the hemorrhagic diathesis is beginning to show itself in the mucous membranes. The patients begin to bleed from the nose, and large, blackish crusts soon form in the nasal cavities, between which fluid blood oozes slowly and in drops. Quite regularly, there is bleeding also from the gums, which then appear, as in the scorbutic, diffusely reddened and softened as well as invaded by hemorrhagic infiltrations.

Larger hemorrhagic infiltrations are formed in many parts of the mucous membranes of the mouth and throat, in which very frequently, in the region of the interstitial exudate, the mucosa breaks down and soon becomes necrotic. In consequence of this, a penetrating *fœtor ex ore* arises, and with the sanguinolent mucus which constantly flows from the mouth are mingled the discolored shreds of dead tissue.

It is remarkable and exceptional, in the midst of all these hemorrhagic symptoms, to observe the behavior of the tongue, which, while thickly coated and covered with blackish crusts, does not usually participate in the hemorrhages ; on the other hand, the occurrence of cough and the expectoration of sputa tinged with blood in the majority of cases announce that the hemorrhagic diathesis has taken possession also of the mucous membranes of the deeper air-passages.

Appetite is entirely lacking from the outset ; and, on account of the incessant retching and vomiting, the patients are usually unable to take

any nourishment, even in fluid form. Unfortunately, also, to add to their other tortures, they are afflicted with the severest thirst. The vomited matter, at first consisting only of stomach-contents, later contains bile, and is usually decidedly bloody. Bloody evacuations also not infrequently take place in the further course of the disease.

The urine is from the first scanty and cloudy ; it nearly always contains albumin, later in considerable quantity, and then it also contains much blood. Its color is then a dirty brownish-red, and the microscopic examination shows, in addition to tube-casts and epithelium, large numbers of red and white blood-corpuscles. In women severe metrorrhagic symptoms are scarcely ever lacking ; and in pregnant women, abortion or premature delivery is the rule.

Such is essentially the development of the pathologic process which is fully completed on the third or fourth day. We have still to add that in purpura variolosa the outbreak of the true smallpox exanthem does not usually occur. At most, isolated papular elevations are found on the skin on the third or fourth day of the disease, if life is prolonged so long. These remotely remind one of the smallpox papules, although even from the beginning they are tinged with blood.

The course of the malady is incessantly unfavorable, and concludes fatally, probably without exception. Usually death occurs within the first four or five days of the disease, and one never sees a real case of purpura survive to the end of the first week. In most cases consciousness is retained unclouded even to the last hours of life, while, with the general exhaustion, pulse and respiration become gradually weakened. A terminal elevation of the temperature has not been observed, and usually at the last the temperature falls to subnormal.

Just as the clinical symptoms and the general course of purpura variolosa present much that is unusual and peculiar, so the postmortem examination also yields anatomo-pathologic findings which are irregular in many respects. (For the latter, compare later under Pathologic Anatomy.)

LITERATURE.

Concerning purpura variolosa consult: Hebra: *l. c.*, page 640 *ss.*—Zuelzer: " Berliner klin. Wochenschr.," 1872, Nr. 13.—Curschmann: *l. c.*, 3. Aufl., S. 164 ff.

Variola pustulosa hæmorrhagica.—This second clinical form of hemorrhagic smallpox is more frequent than the first ; it is also observed more uniformly in the different epidemics. In contrast to purpura, it is seen less frequently in the strong and healthy than in the weak, and it develops especially in inebriates. For the latter reason, men are

attacked more frequently than women; yet apart from the protective influence of vaccination and revaccination, there is no kind of exclusive personal relation. In malignancy, at least in the fully developed cases, it stands scarcely less high than purpura variolosa, though its course is somewhat more protracted.

With regard to the period of incubation, there is no especial difference between this and ordinary variola; the initial stage shows severe symptoms. High fever, delirium, and generally a very intense lumbar pain are present. The peculiarity of this form of the disease, especially its hemorrhagic character, manifests itself, sometimes earlier and sometimes later, but always in the already developed smallpox eruption, hence not before its appearance. At times the hemorrhagic character may be recognized in the papular stage of certain pocks, when they immediately put on or exhibit a purple to black color; somewhat more frequently in the vesicular stage (hence in the stage of efflorescence), and most frequently this occurs in the beginning of and during the period of suppuration. The hemorrhagic change, after it has once begun in such cases, goes on; sometimes rapidly, at other times more slowly; sometimes in smaller, at others in larger, areas of eruption; the change may indeed be but rare, or nearly universal, and accordingly the individual cases for the time being and by degrees naturally assume a somewhat different appearance. In the cases of a more general but at the same time not fully developing hemorrhagic metamorphosis of the exanthem which most frequently occur, it is usually seen first in the lower regions of the body; it originates in the legs, the abdomen, and the buttocks, and thence extends a variable distance upward. The whitish or yellowish color of the vesicles or pustules undergoing the metamorphosis is changed, on account of the blood extravasated into them; they assume a dark, blackish-red, or blackish-brown color, and likewise the crusts and scabs arising on the skin from the discharge of the sanguinolent contents are of a similar color. It is further observed, in cases in which the hemorrhagic change of the smallpox rash assumes greater dimensions, that the hemorrhagic diathesis is still more generalized. In such cases, outside of the region of the original pocks in the skin, smaller and larger blood extravasations (petechiæ and ecchymoses) appear, and hemorrhagic symptoms also develop elsewhere (epistaxis, bleeding of the gums, hematuria, etc.); in short, an acute cachectic condition arises subsequently which, in many cases, reminds us of purpura, and, like it, leads inexorably to death.

But even when this does not happen, and when the hemorrhagic diathesis remains limited to the exanthem, the disease is in most cases fatal.

This is true even in those cases in which the hemorrhagic change occurs late and is limited to small areas.

This bad condition may be ascribed to the fact that the last-named cases of variola pustulosa hæmorrhagica usually are very severe in and of themselves, and generally assume an adynamic character very early. Under all circumstances we have to assign a very ominous significance to the events described above, and this should be especially heeded with regard to the prognosis.

My own experience in relation to variola pustulosa hæmorrhagica fully justifies me in assigning to it a very bad prognosis. Almost without exception, I saw patients die very quickly as soon as the exanthem became at all extensively hemorrhagic.

The anatomo-pathologic findings in variola pustulosa hæmorrhagica are in many respects like those in purpura variolosa ; in other cases, however, they are somewhat different. (Compare later under Pathologic Anatomy.)

After finishing the description of those kinds of variola which may be regarded as especially malignant types of the disease, it now remains to give a brief description of the mild and abortive forms of smallpox— varioloid and variola sine exanthemate.

Varioloid.—Varioloid * (or variolois) is a name given, since Thomson,† to the mild type of variola as it is usually observed in persons who have been vaccinated and revaccinated, but who have passed beyond the period during which inoculation grants absolute protection. It is characterized anatomically by the fact that the typical exanthem on the skin, either wholly or in by far its greater part, undergoes only superficial changes and, in consequence, leaves no lasting stigmata (scars). Clinically it is recognized by the absence of a severe, febrile, suppurative stage, by the slighter intensity of the symptoms in the mucous membranes, and by the correspondingly shorter and milder general course of the disease as opposed to variola vera. Notwithstanding all this, varioloid and variola vera have the same etiologic origin, and are not essentially different from each other. This is made somewhat clearer from the fact that connecting transitional grades exist between the two, as well as from the

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* I give the preference to the term "varioloid" for the mild form of smallpox, although the name "variolois" is the more usual term for it. The latter word is, as F. v. Hebra has rightly emphasized, an etymologic monstrosity, and on this account should be eliminated from the scientific nomenclature of the disease. Valid objections might also be raised against the term varioloid, since the affection so characterized is not *like smallpox*, but *is* smallpox.

† *Loc. cit.*

further fact that each can be acquired interchangeably by infection from the other (compare Definition of the Disease).

The circumstance that at the present time, in very many civilized countries, vaccination and revaccination are generally practised gives to the cases of varioloid in these geographic and political regions a very decided numeric preponderance, as a rule, in the epidemics which now occur. The immediate consequence of this condition is a very considerable decrease in the mortality from smallpox as compared with former times. However pleasing this fact is in itself, and however convincingly it speaks for the conspicuous value of vaccination, it has, nevertheless, led not a few into a mistaken idea of the real nature of varioloid. In fact, of late many have wished to regard it as an artistic imitation of smallpox, created by vaccination, and which did not exist in prevaccination times. So also the terms " modified " or " mitigated " smallpox have arisen for varioloid, in both of which terms is included the idea that this mild form of smallpox is always and without exception artificial. Against this view we must enter a decided protest, for it is contradicted by historic facts. From the latter, it appears that in the prevaccination period also light cases (of the character of varioloid) were associated with severe ones at all times and in all epidemics ; and, further, that there were also, though more rarely than at present, epidemics in which the milder cases were more prevalent than the severe ones. Accordingly we cannot believe that varioloid is to be regarded as a modification of smallpox of recent date, and merely called forth by the process of vaccination. Not only the natural predisposition to the disease, but also at times the virulence of the smallpox virus, must have been variable in former times to cause those differences of intensity which have been already observed. The difference, however, between former times and the present consists in the fact that by vaccination and revaccination a third and, indeed, a determining factor has been introduced, so that in those who have been vaccinated and revaccinated, in case of the acquisition of the disease, the artificially diminished predisposition suffices for acquiring varioloid only.

In sharpest contrast to this theory stands, of course, that other idea, according to which the undoubted preponderance of varioloid in recent times is said to have nothing at all to do with vaccination and revaccination. According to this idea, which still lurks in the heads of the antivaccinationists, the smallpox virus, or the natural susceptibility to the disease, or both together, have, in the course of the nineteenth century, undergone a spontaneous weakening process, and therefore the disease is now milder and less dangerous. We can imagine no greater error ; one

need only read the reports which still come in of the devastations of smallpox among unvaccinated peoples who are lacking in European culture to see immediately that these data alone entirely destroy that false theory.

From all that has been said, the pathogenesis of varioloid may be stated in this way—the mild form of smallpox is not entirely an artificial product, still less is it entirely a natural product. As a fact, many cases now owe the mild character peculiar to them to an after-influence of the protective vaccination, and thus far possess the characteristics of " mitigated " or " modified " smallpox, understood *cum grano salis*—a relative justification, at least, for the term varioloid.

The usual course of a case of varioloid is as follows : The stage of incubation presents no peculiarities ; the disease generally begins, as does variola vera, quite suddenly. The initial stage, on the other hand, more frequently departs from the regular form in so far as greater fluctuations of intensity and development occur in individual cases. Fever, delirium, and the other combinations of initial symptoms are often as violent as could be wished.

In other cases of varioloid the initial stage runs a relatively mild course, much milder than is ever observed in severe cases of smallpox. The occurrence of a measly initial exanthem (or rash), which has been often observed, although the observations have been collected in only a few epidemics, is to a certain degree peculiar to a beginning varioloid, because this form especially is seen only exceptionally in the initial stage of variola vera. (Compare the description given earlier.) The differences between mild and grave variola (varioloid and variola vera) become more decided with the eruption of the smallpox exanthem, —that is, in general from the end of the third day of the disease,—and from that on, the differences are found at least as much in the general as in the local symptoms.

The condition of the body-temperature and the general condition are pathognomonic for decided cases of varioloid. Immediately with the first appearance of the smallpox exanthem on the skin the fever begins to abate, and the fall of the temperature is generally so rapid and so complete that on the fourth day of the disease complete apyrexia has already made its appearance. (Compare, on the other hand, variola vera.) This crisis of the fever is followed in the typical cases of varioloid by no further rise of temperature ; hence it is definitive. With the rapid lowering and complete disappearance of the fever all other disturbances of the general condition immediately abate, and generally so rapidly that usually from the fourth day on, a real and lasting feeling of well-being

exists. Only certain local discomforts remain, caused for a short time by the exanthem on the skin as well as on the mucous membranes which are attacked ; but these are generally not very important.

In many somewhat severer cases, which may, in addition, be observed as transition forms or intervening types between varioloid and variola vera, the fall of the fever takes place, not in a single line, but, with a slight evening interruption on the fourth day, forming a so-called *crisis protracta*. Such cases usually resemble somewhat more closely the cases of variola vera, in so far that as the other general symptoms in them disappear more slowly, so also the exanthem in its outbreak follows more closely the regular order of variola vera, and, also, in its further course
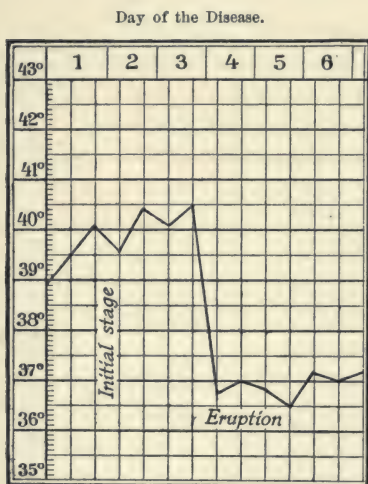
Fig. 8.—Varioloid with high initial fever and sudden fall of temperature at the beginning of the eruption.
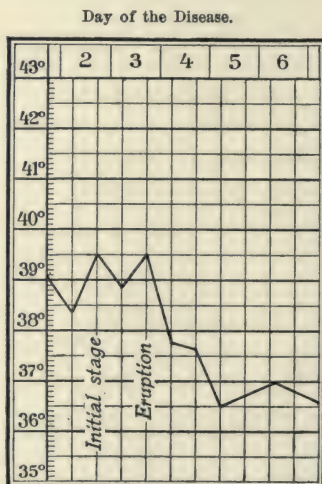
Fig. 9.—Very mild case with slight initial fever and sparing smallpox exanthem (few, quite scattered pustules). Twenty-seven-year-old nurse, vaccinated only as a child.

some trace of a suppurative fever may be seen. Finally, it is not altogether impossible that, from such hybrid forms of smallpox, in spite of their generally favorable course, true smallpox scars may be left after recovery

The usual course of a varioloid fever is satisfactorily illustrated in the temperature curves shown in figures 8 and 9.

The outbreak of the exanthem, in varioloid, begins at the usual time (somewhat after the third fever elevation), but in the further course it differs more or less from the rule applying to variola vera, and hence is atypical to a different degree in the various cases. Although in cases of varioloid the pocks show some preference to appear first on the head

and face, and usually are most abundant also in these places, yet this is not always the case, but, on the contrary, there are numerous exceptions in both respects. The number of pocks is likewise extraordinarily different in different cases. In the lightest of all cases, which form the clinical transition to variola sine exanthemate (compare the later description), the eruption is in general so sparse that it is at times difficult to find half a dozen papules or a few more on the whole surface of the body. In the more fully developed cases, on the other hand, the whole skin from above downward is, at the end of the eruptive stage, plentifully sprinkled with the pocks. The duration of the eruptive stage is, in general, distinctly shorter than in variola vera, and lasts on an average not more than two days (about forty-eight hours), so that nearly always by the end of the fifth day of the disease the whole number of skin pocks is definitely reached.

Much oftener than in variola vera there are, within the short period of the eruption, all kinds of small irregularities; above all, subsequent crops in those portions of the body in which the pocks had already appeared extensively earlier in the disease. Through all these variations from the normal course of variola vera the varioloid eruption is impressed, on the one hand, with the character of prematurity; and, on the other, as already remarked, with an atypical character. The same thing may be said of the course of development of the individual skin pocks. Reddish points first appear in varioloid in the affected portions of the skin, which then grow to reddish papules; the further course is, however, quite irregular. We observe quite frequently that a smaller or larger number of the pocks in varioloid remain at the papular stage of development, without passing into the stage of maturation; such rudimentary or abortive pocks are the first to undergo retrogression. Others are likewise arrested in their development, but somewhat later, in the beginning of the vesicular stage; and then in this form, without further development, dry quickly to small, brownish crusts; still others finally reach complete development; they, like true smallpox vesicles, frequently show, in this stage, the central depression (or smallpox umbilicus) already described, and the abundant fluid contents, which were at first clear, become turbid. This whole process does not lead to decided suppuration, however, even in the last-named perfectly developed pocks of varioloid; the changes occur more quickly than in the corresponding forms of variola vera, and, in the second place, the beginning of desiccation occurs immediately after the suppuration. Thus, in typical varioloid the process does not generally extend to a deeply penetrating suppuration in the corium, with its other accom-

panying symptoms, the severe inflammatory congestion in the region of the pocks, the suppurative fever, and the other symptoms of secondary toxemia.

On the mucous membranes, also, the pathologic change is far milder and more propitious in varioloid than in variola vera. The number of the individual pocks which can be seen is usually very small, and often even vanishingly small. The accompanying catarrh is, to be sure, never quite absent, and it is not infrequently rather more severe than would be expected from the insignificant development of the exanthem in the mucous membranes of the mouth, throat, etc. But it always restrains itself so far as its intensity and distribution are concerned within certain limits, and therefore only exceptionally causes the patient any more serious trouble. More deeply penetrating suppuration in the throat, larynx, or elsewhere, or purulent metastases in the internal organs, do not occur in varioloid.

The desiccation of the cutaneous eruption not only begins early, but also advances rapidly ; so also the crusts, on account of their superficial position, are in most places very loosely attached ; and in consequence of this, aided by the abundant new formation of the epidermis, are early loosened. By repeated baths and other mild measures we can easily succeed in separating them more quickly than would otherwise be the case. Only on the palms of the hands and the soles of the feet does the complete separation of the lentil-shaped granulations embedded in their thick epidermal capsules usually take somewhat longer in varioloid than is agreeable to the wishes of the impatient convalescent, who has, in the mean time, as a rule, perfectly recovered, and is, aside from this circumstance, in good spirits.

Where the crusts fall off or are not removed too early, there appear at first pigmented areas, with a complete epidermal covering ; these may be flat or slightly elevated ; scars, on the other hand, are nowhere left behind. Individual variations from this rule of course occur in many cases of varioloid, but they are in general irrelevant ; while these cause a few permanent scars in their further course, they are scarcely disfiguring. The well-known elevations, which owe their existence to the remnant of inflammatory swelling of the papillæ, quickly become entirely level, as a rule ; the brownish pigmentation lasts somewhat longer, but it, too, completely disappears after a few weeks.

In rare cases the small elevations persist somewhat longer in many places. In these cases we may observe for some time on the upper surfaces of the papules a locally increased production and collection of sebum (seborrhœa variolosa). This deviation from the customary heal-

ing process of varioloid, which likewise perfectly disappears in time, is commonly known as " variolosa verrucosa" (English " wartpox ").

Another anomaly is still more infrequent. If the fluid contents of a pock undergo absorption unusually quickly and the capsule does not collapse with corresponding quickness and completeness, then the space may in the interim be filled from without or from within with air. Such air-containing capsules, which for a time after varioloid sometimes remain on the skin from the exanthem, were formerly and are still called " variolæ siliquosæ," or " pod-pocks" (" Hülsen-pocken ").

Variola sine exanthemate.—That the eruption may be very scanty in especially mild cases of varioloid has been already mentioned. But always, in those cases, the existence of some typical pocks at least guaranteed that a case of smallpox was really present. But in times of smallpox epidemics cases are sometimes observed in which a variolous disease must be assumed, although no trace of a smallpox exanthem appears anywhere on the skin. We characterize such cases as " variola sine exanthemate "; they are perfectly analogous clinically to those cases of measles and scarlet fever without the eruption—a condition which is characteristic of those diseases (morbilli, aut scarlatina, sine exanthemate).

The proof that in such cases a variolous process is really present is usually to be sought for both in the etiology and in the symptomatologic factors. The affected individuals have, as a rule, been known to have had the opportunity of being infected ; in other words, they have, with natural susceptibility to the disease, been directly or indirectly brought into contact with variola patients. They were attacked, after a time corresponding to the known period of incubation for smallpox, with symptoms which correspond to the initial symptoms of variola (fever, lumbar pain, delirium, and perhaps initial rash), so that the outbreak of a smallpox exanthem was certainly to be expected. Nevertheless such an eruption did not appear, although after a course of three days the fever of the patient rapidly abated, with complete restoration of his normal general condition. In such cases, which actually do occur, one is not able to avoid the assumption of a variolous process which ran an abortive course without reaching the development of the exanthem. At other times, less frequently, the assumption of a preceding variola sine exanthemate may be based, with less certainty no doubt, on its own antecedents rather than on its later consequences of an attack. A dubious case, with high fever and all kinds of toxemic symptoms, which did not for the moment admit of certain diagnosis, became, after a few days, free from fever and well ; after the proper time persons in his neighborhood

were attacked with true variola. Also under such circumstances it is more than probable that that doubtful case was a case of variola sine exanthemate, especially if subsequently an antecedent communication with smallpox patients or their effects can be in any way shown. Such cases of variola sine exanthemate are at times a sufficient proof for the fact that variola is contagious even in the initial stage, and that the exanthem is not necessary to constitute infectiveness (compare Etiology).

I myself, many years ago, met with a striking example of this kind. A female peddler, with high fever and other general symptoms, was brought to the clinic of F. von Niemeyer at Tübingen at the time when I was studying there; in the course of three days she became fever-free. The diagnosis remained doubtful until twelve days after the admission of this woman, when 3 patients in the same ward, who were detained in the hospital of Tübingen on account of some chronic disease, were attacked simultaneously at night with high fever, which lasted for three days and was then followed by the appearance of a varioloid exanthem. In Tübingen and the near neighborhood variola was not at that time prevalent, but it was learned later that the peddler had come from a smallpox neighborhood.

The course of variola sine exanthemate is favorable throughout; a description of its symptoms may be omitted, as they are identical with those of the ordinary initial stage of variola, and the whole disease is in these cases reduced to such an initial stage.

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Concerning variola sine exanthemate, consult: Bierwirth: "Archiv der Heilkunde," Bd. xiii, S. 226 ff.

COMPLICATIONS AND SEQUELS.

The variolous process is extraordinarily rich in complicating disturbances of different kinds. Most of these disturbances do not develop before the period of the full development of the exanthem is reached. These disturbances occur much more frequently during the period of suppuration and toward its close, while, during the period of desiccation and afterward, they again become less frequent. On all this depends also the fact that complications occur out of all proportion more frequently in cases of fully developed smallpox (variola vera and especially variola confluens) than in varioloid. This circumstance weighs heavily in the prognostic scales, for the complicated forms of smallpox, according to all experience, add a very considerable contingent to the general mortality as well as to the number of cases of incomplete recovery.

Many of these so-called complications of variola are in reality noth-

ing more than either extensions of the purulent inflammatory affections of the skin and mucous membranes *per continuum* to neighboring regions, or purulent metastases to other more distant parts. By this is explained, in part at least, the above-mentioned difference, since complications so caused occur *eo ipso* predominantly in the fully developed cases of smallpox and in the suppurative stage. Other complications do not possess this purulent character, and for these the principal difference mentioned is naturally lacking apparently *à priori*. But experience teaches that the majority of these complications also occur much more frequently in severe forms of smallpox than in mild forms, and that therefore in practice it is not necessary that they be considered entirely separately. If one considers, moreover, that the shock to the general constitution in variola vera, and still more in variola confluens, is undoubtedly far more intense than in varioloid or in variola sine exanthemate, then one can easily explain why the vulnerability of the organism to all possible injurious influences must be much greater in the former than in the latter.

This increased susceptibility, which during the attack of variola so frequently gives the impulse to complications, also continues for some time into the convalescence from variola, and thus causes the occurrence of sequelæ of a milder or graver type, in which also variola is especially rich. What has been said of the complications in particular is also true concerning these subsequent disturbances—namely, that they occur much less frequently after varioloid than after variola vera or variola confluens.

Although, strictly speaking, there must be differences between complications and sequelæ, yet the boundaries between the two are frequently effaced in practice, and the end of the real disease and the beginning of convalescence in severe cases of smallpox are only indistinctly separated from each other. Also it happens frequently that certain disturbances which are complications at first do not reach their full clinical development until later in the stage of convalescence. For these reasons, in the following description complications and sequelæ will be described together, and, for the sake of simplicity and comprehensiveness, will be classified according to their anatomic location.

The skin is not only the principal field for the specific variolous changes, but very often in severe cases other and very extensive processes occur in it, either simultaneously with or subsequently to the eruption. Of acute bedsore we have already spoken cursorily ; in higher grades of suppuration, in spite of the most careful attention to the patient, it often cannot be avoided on the buttocks and other dependent

portions of the body. If it becomes firmly established, as, unfortunately, often happens, it may threaten life itself, and in every case delays to an extraordinary extent the definite recovery of the patient.

Independently of position and of the mechanical force of pressure, acute gangrene of the integument in larger or smaller areas may develop in severe cases of variola discreta and in those of variola confluens at the height of the suppurative process, as a consequence of a complete stasis of the blood in the region of much increased inflammatory congestion. These cases are generally quickly fatal, before a line of demarcation has formed; in the rare exceptions of improvement and ultimate recovery, there remain, after the removal of the gangrenous portions, corresponding areas of granulation tissue, and finally, of course, extensive scars. Likewise injurious, and at the same time much more frequent, are erysipelas and phlegmons, which usually set in suddenly with high fever at the close of the suppurative period or during desiccation, and are not infrequently fatal. The excoriation of the skin, which is present to some extent, manifestly plays an important part in their causation. Less dangerous, indeed, but extremely troublesome, is furunculosis as a sequela, which, under certain circumstances, runs an incredibly protracted course, and may for months recur again and again. Finally, in many who have recovered from smallpox there remains for years, especially in the face, but also in the back and other portions of the body, a tendency to acne-like eruptions, which are probably etiologically connected with retention of the sebum (in consequence of retraction of the scar tissue of the skin and obstruction of the mouths of the sebaceous glands).

The respiratory apparatus is likewise very frequently attacked by complications. Apart from the acutely destructive processes in the larynx (perichondritis laryngea), which in most cases are quickly fatal, or, in more fortunate cases, leave behind, after they have healed, all kinds of organic defects in various places and positions, as well as permanent phonic-respiratory disturbances, pneumonic affections very often occur in the lungs in severe cases of variola. These complications generally consist of lobular and hypostatic forms of pneumonia, less frequently of abscess of the lung as an expression of metastasis, and most rarely the ordinary lobar pneumonia as an accidental coincidence with the existing variola. All these pneumonic affections are, of course, more or less dangerous and serious accidents in the course of a case of smallpox; when they occur, they are comparatively often chiefly responsible for the fatal termination of the disease. On the part of the pleura the patient is threatened, at the height of the disease and during the course

of the suppurative process, with the occurrence of inflammatory exuda-
tions which nearly always undergo a rapid transition into the form of
empyema, doubtless, in all cases, of metastatic origin.   These empyema-
tous processes in variolous patients tend in a great degree to a malig-
nant course ; once begun, they develop rapidly, even at times most
acutely, and to a very considerable extent.   On account of this violent
course, which, as it seems, is not checked by any therapeutic measures
(operative interference), they are, without exception, in a short time
fatal to the patient, who is already hard pressed by the principal disease.

Rarer than the purulent pleuritis is pericarditis, partly in connection
with the former and induced by it, and partly as an independent com-
plication.   Endocarditis ulcerosa has also been observed in individual
cases, and is generally found at the postmortem examination.   Of affec-
tions of the rest of the vascular apparatus, marantic thromboses (in the
femoral veins) must be especially named ; they occur quite frequently in
the later stages of variola, as in other severe diseases.

Of complications in the region of the digestive organs, we may espe-
cially name parotitis and acute inflammatory processes in the salivary
glands in general.   Such complications were observed in many epidemics
in large numbers ; in other epidemics, either seldom or never.   The
usual outcome was, as is common in the symptomatic forms of this affec-
tion, the formation of abscesses within the glands which are thus attacked.
Diphtheritic-like membranes are often formed in the region of the soft
palate and in the throat.   This complication is by no means uncommon in
certain forms of smallpox ; it is, as I, with Curschmann, would emphasize
after some experience, met especially, and even with more constancy, in
the hemorrhagic forms of variola (purpura variolosa and variola pustu-
losa hæmorrhagica).   Finally, in some European smallpox epidemics of
earlier historic date very severe cases of a dysenteric type seem to have
played a prominent part in the course of the disease and to have been
the origin of one of the oldest names of variola which has come down
to us, " morbus dysentericus cum vesicis " (Gregor von Tours).   Syden-
ham also distinguishes, at least as a special form of the disease, a
" variola dysenterica " ; on the other hand, no decided reports of this
kind have come to us from later times.   Simple diarrheic evacuations
(not of a dysenteric character) were certainly observed (among recent
authors) by Trousseau, and actually in the beginning of the disease ;
for the rest, all reports of modern authors agree far better and with tol-
erable uniformity in noting an inertness of the intestinal movements and
constipation during the whole course of the disease.

The nervous system is in variola comparatively often and after a

manifold fashion the seat of complications and sequelæ; the occurrences observed are, from a clinical standpoint, especially interesting. At all events it would seem as if the process of variola possessed in a prominent degree the power to awaken the latent predisposition to nervous affections, as well as, on the other hand, to create, quite directly, neuropathies. The diseases observed affect all possible provinces of the nervous system (brain, spinal cord, and peripheral apparatus); they are partly of the gross-anatomic kind, in part purely functional, while in other cases their position and nature appear, in the lack of postmortem evidence, still doubtful until after further investigation. In contrast to the majority of the other complications and sequelæ of variola, not a few of the affections belonging to this group are not strictly confined to certain stages of the disease itself and of its immediate legacy, and are not at all related to the severity of the individual case; they maintain, rather, in both respects a quite remarkable independence. From all these statements this much seems to be very well established, that here is a very wide and fruitful field for further investigations.

The facts that have been observed are essentially as follows: Delirium of the common kind and coloring forms so frequent a symptom of the initial stage as well as of the stage of suppuration that it may be considered as a part of the disease itself. It is, however, somewhat different from the delirium which is specifically colored and is combined with tremors, the *delirium alcoholicum* or *delirium cum tremore*, which occurs very frequently in inebriates when they are attacked by smallpox. In consequence of this, it is observed in variola vera as well as in varioloid, in the two distinct chief types of the disease, oftenest at the time when, after the initial stage, the fever abates and the exanthem appears. It possesses in all cases a very grave significance, and may be fatal on account of the accompanying exhaustion, when the attack of smallpox was otherwise rather mild. As sequelæ of variola of every grade, but less frequently than after typhoid fever, influenza, and acute rheumatism, psychoses occur, which are usually of a melancholic character, and in most cases have a protracted course. In spite of this, the prognosis in these cases is usually favorable. Perhaps in this category of the functional diseases of the brain we may place the extremely isolated observations on diabetes mellitus which developed in the convalescence from smallpox (Friedberg, von Frerichs) and was permanent in its nature.

To the gross-anatomic lesions in the region of the brain belongs, in the first place, purulent meningitis, the relations of which to the smallpox process on the skin are probably metastatic. It is fortunately a rare compli-

cation of variola, seems to occur most frequently in childhood (Gregory), and is especially connected in its occurrence with the period of suppuration and of beginning desiccation. Likewise rare, but occasionally observed on postmortem examination, are localized encephalitic diseases of heterogeneous and also non-purulent character (E. Wagner), and also simple areas of softening and blood extravasation. These complications many a time remain latent through life and are first discovered at the autopsy; at other times, however, they announce their presence during the lifetime of the patient by the sudden occurrence of hemiplegic symptoms. Whether the aphasias which have been repeatedly observed during the course of variola (Curschmann and others) likewise belong to this category is doubtful, as postmortem examinations are lacking; the transitory character of these disturbances of speech suggests, in the cases seen hitherto, the possibility that these may just as well depend upon purely functional alterations of the speech centers.

In greater degree than the brain is the spinal cord involved in the complications and sequelæ of variola; the symptoms observed hitherto have been mostly paraplegias of the motor kind. These paraplegias are not limited to severe cases of variola, but seem to occur as well in cases of varioloid. They have been observed—which is worthy of note—in every stage of the disease, from the initial stage to the far-reaching period of convalescence from variola (Gubler); even before the proper beginning of the disease, in the stage of incubation, they have been separately noted (Leroy d' Étiolles). The beginning of the paraplegic paralysis is usually sudden, subacute, the paralysis often remaining limited to the lower portions of the body. The bladder and rectum may be involved so far as their motor functions are concerned, while the sensibility of the affected regions usually remains undisturbed. The paralysis, once started, shows a rapidly ascending character, and also the clinical symptoms of Landry's paralysis (Gubler, Bernhardt, Leyden, Chalvet, Gros, Oettinger, and Marinesco); these cases, as a rule, are fatal after a short course. More rarely than acute paraplegias, acute ataxias are observed (Westphal); still more rarely acute monoplegias, which, in their clinical behavior as well as on account of their occurrence in children, present the picture of acute spinal infantile paralysis (paralysis infantum acuta) (Damaschino).

With regard to the real substratum of these variolous myelopathies, in a portion of the cases at least, there can be no doubt that they are connected with the development of a myelitis occurring in numerous small patches (that is, an insular or disseminated myelitis) (Westphal). According to the number, the location, and the extension of these masses

in the spinal cord and medulla oblongata, the clinical symptoms natu-
rally vary in the different cases. That especially typical pathologic
pictures of Landry's paralysis may in variola exist in combination with
the disseminated myelitis of the kind just mentioned seems, according
to a very recent communication, to be firmly established on an anatomic
basis (Oettinger and Marinesco). As regards other cases of ascending
paralysis, formerly as well as recently, in which the direct anatomic
proof of a disseminated myelitis is lacking, other possibilities concern-
ing their origin naturally remain open (an acute infection through the
entrance of the pathogenic micro-organisms into the spinal cord, a poly-
neuritic origin, etc.). In brief, we may apply to them all the other
theories and eventualities which are claimed as an explanation of Lan-
dry's symptom-group.

As neuropathies which, on account of the very limited topographic
extension of the resulting clinical disturbances, are very probably
related to certain anatomic or functional alterations of special peripheral
nerve-areas the following might be named : post-variolous paralyses of
the soft palate and pharynx (Leyden, Curschmann), which are quite
analogous to the much more frequent diphtheritic paralyses of these
parts ; also of paralysis of single muscles, like the deltoid (Curschmann),
and limited cutaneous anesthesias, and the like.

The higher organs of sense, the eye and ear, participate to a very
marked degree in the accompanying and subsequent disturbances of
variola. The mechanism of hearing is most frequently attacked, its
share in severe cases of the disease being extremely great (Wendt).
The diseases of the ear which occur usually begin during the stage of
suppuration. These troubles generally arise from a purulent catarrh of
the Eustachian tube, which is an almost constant symptom of the period
of suppuration of variola gravis and is genetically connected with the
variolous affection of the throat. Through extension of the inflamma-
tory process in the tube to the middle ear, especially to the labyrinth
and the substances of the petrous bone, there may often arise, earlier or
later, the pathologic conditions in the auditory apparatus and its imme-
diate surroundings known collectively as otitis media, otitis interna, and
caries of the petrous bone, with their objective symptoms, which will
be described more in detail. It is in the nature of these affections of
the ear that they usually last longer than the variola itself, at times even
for life, and likewise that they often cause difficulty in hearing or even
complete deafness in the affected ear. Moreover, by extension of the
process to the membranes of the brain, and to the brain itself, these
affections may, even after many years, suddenly endanger life itself.

In prevaccination times serious diseases in the mechanism of sight and lasting defects in the region of the eyes were frequent and at times very sad results of smallpox. In recent times they have fortunately become rarer in comparison to the still considerable number of ear diseases of variolous origin; they are not yet, however, absolute rarities (Adler). It is observed that the conjunctivitis which is regularly present, instead of abating at the close of the variola, persists and takes on a chronic character. At the height of the disease—that is, in the stage of suppuration—in severe cases of variola, and still more in variola confluens, keratitic processes may arise through extension from the connective tissue to the neighboring structures; less frequently iritis and choroiditis may occur, but these last, as a rule, only when, in consequence of the presence of keratitis, perforation of the cornea results. In especially serious cases even panophthalmitis may develop, leading to phthisis bulbi. In hemorrhagic variola, in addition to the ordinary conjunctival hemorrhages (compare the earlier description), hemorrhages may also occur in the interior of the eye, which most frequently originate in, and are located in, the retina. As results of the above-named changes, we may name among others the following: Opacity of the cornea (leucoma), iritic adhesions, and formation of coloboma; all these are accompanied by corresponding limitations of the power of vision.

It has already been mentioned in the description of the course of the disease that eruptions of smallpox on the conjunctiva bulbi, according to the common significance, are the extremest rarities, and that they are not common occurrences even on the conjunctiva palpebrarum. On the other hand, the external skin of the lids often takes part in the skin eruption and also in the after-consequences of the same. In this way permanent deformities of the lids may be caused on account of scar-formation; namely, ectropion, which is not only very disfiguring, but, on account of the incomplete closure of the lids, may prove a constant source of danger to the eye which is left thus unprotected.

Pathologic changes in the region of the nose are likewise observed in certain cases, but are not, on the whole, very frequent. The deformities and mutilations of the alæ nasi which often remain after confluent pocks in the face form a single exception. After such cases of variola confluens, as a result of extensive ulcerations of the mucous membranes, scar-like contraction or even complete obliteration of one or the other nostril may sometimes develop. By changes of the kind last mentioned, the respiratory function of the organ is, naturally, first impeded, but likewise its capacity for the reception of odors is affected to a variable extent.

Concerning the motor apparatus, muscular abscesses and inflammations of the joints, most frequently attended with purulent exudations into the joint cavity, are to be mentioned as complications of variola. Both are to be regarded as metastases and, corresponding to this their nature, are not rare occurrences in severe cases of smallpox at the close of the period of suppuration. Among the joints, the larger ones, especially the shoulder-joint, and next to this the knee-joint, show a certain predisposition; yet it also happens that several joints are attacked simultaneously or in rapid succession. Very rarely, but yet now and then, we meet acute arthritic processes in cases of varioloid; in such cases, however, the peculiar exudation is either wanting or it remains benign—that is, it is simply serous in character. Concerning a peculiar osteomyelitic disease of variola, which, to all appearances, has not the significance of a complication, compare Pathologic Anatomy, under Postmortem Findings, in what follows.

Complications on the part of the kidneys have also been observed, but are not frequent. We of course except a slight degree of albuminuria which is very often present in the initial stage as well as in the stage of suppuration, but which is entirely analogous to that observed in other febrile, infectious diseases—the so-called febrile or hematogenic albuminuria. Less frequently are seen, on examination of the urine, signs of a real nephritis as a complication (high degree of albuminuria, very abundant tube-casts, etc.). Moreover the cases of purpura occupy a special place, and in it the urine quite regularly shows certain typical alterations (compare the earlier description).

The more important complications on the part of the female genital organs have already been mentioned in another place. We may merely repeat here that the normal termination of menstruation is delayed by the beginning of variola; that pregnancy is, as a rule, quickly interrupted; and, finally, that in hemorrhagic cases the uterine mucosa, in its own characteristic manner, takes part in the hemorrhagic diathesis. Whether alterations pertaining to the ovaries and their adnexa occur in variola, has not yet been fully decided.

On the other hand, a real disease occurs in the testes, which seems to be more than a mere complication of variola. For further particulars concerning this variolous orchitis, which is analogous in many respects to the above-mentioned variolous osteomyelitis, compare Pathologic Anatomy, under Postmortem Findings, in what follows. So far as is now known, however, no special clinico-symptomatologic significance seems to be attached to these peculiar affections of the testes in variola patients.

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PATHOLOGIC ANATOMY.

HISTOLOGIC STRUCTURE OF THE VARIOLOUS POCKS IN THE SKIN AND MUCOUS MEMBRANES.

WE have only rarely the opportunity to study anatomically the various changes which the local irritation of the smallpox virus excites in the skin. These changes, according to Bärensprung, consist of a very circumscribed hyperemia corresponding to the location of the future pock, with swelling of the tissue of the cutis, which becomes distinctly recognizable in the papillæ, but can be followed through the whole thickness of the cutis to the deep connective-tissue layer of the pars reticularis corii. Immediately, however, local alterations become noticeable in the region of the deeper epidermal layer, in which especially the variolous process becomes localized. Concerning the point of origin and the nature of these latter alterations, however, in spite of the great number of investigations made on this point, many very considerable differences of opinion exist. While the older workers on this subject (Bärensprung, Auspitz, v. Basch, Ebstein, Rindfleisch), and also certain of the more recent investigators (Unna, Touton, Renaut, Leloir, Buri), regard the variolous changes in the epidermis from the beginning as merely the expression of an acute inflammatory process, and differ in their views regarding the further localization and development of this process, Weigert, on the other hand, regards the primary variolous change in the epidermis as non-inflammatory. He considers it rather as a necrobiotic or diphtheroid change caused by the direct local influence of the smallpox virus; groups of living cells in the deep and middle layers of the epidermis are attacked by this change, the inflammatory changes in the immediate neighborhood of the necrotic pock masses are added later. The diphtheroid change begins, according to Weigert, in the rete Malpighii, radiates from it into the uppermost cells of the prickly layer and the horny layer, and develops in the following manner: The cells attacked show, at first, a fine granular cloudiness, the nucleus becomes indistinct and soon disappears entirely. The opaque, non-nucleated structures now for the most part fuse into irregularly formed, clod-like masses, with numerous outrunners upward and laterally, which are sharply separated from the still intact neighboring cells, and altogether form a central framework or reticulum for the

future individual pock. Around such a central pock-mass in the larger pocks, different additional side masses may originate in the near neighborhood of the first; this is by no means ordinarily or necessarily always the case. Soon after the primary changes described have occurred and have reached a certain development, new, secondary appearances become noticeable, which are probably inflammatory in character. These consist in part of an exudation of fluid into the fine-meshed reticulum formed by the diphtheroid process, and in part of an exuberant proliferation of cells in the whole region of the border zone, in consequence of which the central region of the pock soon appears to be surrounded by a wall of cells. Among these proliferated cells of the deep and middle epidermal layers are found, besides the smaller cells, also numerous larger ones and polynuclear forms, and even true polynuclear giant-cells; at the same time, the great proliferation of cells in the region of the peripheral wall of the pock causes the horny layer of the epidermis to be pushed up, and thus a macroscopic papular elevation or smallpox papule develops in the part of the skin affected. This so-called papule is in reality not a solid nodule, but rather conceals in its interior from the very beginning the diphtheroid reticulum just mentioned, with numerous small spaces into which already traces of the fluid exudation have been poured.

The further development of the individual pocks into a multilocular vesicle, which is accomplished in a great many of the pocks during the period of full development of the exanthem, is brought about in reality by increase of the fluid exudation, which is poured in larger and larger amounts into the meshes of the reticulum; these widen more and more, the walls, becoming thinned through pressure, break through in many places, and thus still larger chambers or cavities are formed. The central depression (or the smallpox umbilicus) in the stage of full development of a fully developed smallpox vesicle is easily explained as due to the wall-like elevation of the border zone in consequence of the cell proliferation there; at the same time, it is evident that, wherever a pock has established itself near the mouth of the excretory duct of a skin gland, especially of a hair follicle, the latter then forms a real retinaculum (Rindfleisch) for the central part of the pock covering (or pock-hood), and that under such circumstances the pock-navel generally corresponds directly to the place of exit of such a canal (especially at the site of a hair).

The conclusion of Weigert, according to which the primary origin of a skin pock is not inflammatory, but rather diphtheroid in character, is, according to his report, supported by peculiar findings in certain in-

ternal organs (liver, spleen, kidney, and lymph glands) which are said
to be like the diphtheroid masses in the skin (compare particulars under
Postmortem Findings), and accordingly to be regarded as specifically
variolous. But this whole theory of Weigert is based on the hypothesis
that the diphtheroid changes not only actively and early occur in the
region of the variolous skin areas, but that they are met with quite
regularly at the very beginning.

Both these points have recently been discussed from the other side,
and the existence of the diphtheroid changes in the skin (Unna), as well
as especially their regular and primordial occurrence (Buri) in the
immature smallpox eruption, have been denied. On this account the
question has naturally arisen anew whether the specific influence of the
smallpox virus on the cells of the skin and other organs directly
attacked by it must necessarily lead to necrosis, and whether the necro-
biosis which is in fact often observed is not accidental, perhaps the
result of an exceptional virulence of the smallpox virus (Buri). The
latest investigators, like the older ones, are generally inclined to
consider the local processes in the skin as inflammatory, and particu-
larly to attribute the central stroma of the pock to the compression by
inflammatory exudation of the prickle cells, which are at first paren-
chymatously swollen and then compressed by the accumulating exudate
between the middle cell-layers of the epidermis. According to this
view, as can readily be seen, the local process in the formation of
a skin pock is in its genesis reduced to an inflammation, which, aris-
ing from the cutis, and immediately attacking the epidermis, caused
in the latter partly parenchymatous and partly exudative changes, and
which, in the border zone of the individual pock, gave the impulse
to a proliferation of cells, such as has been already much more fully
described above.

Among the parenchymatous changes of the epidermal cells which
subsequently result from the swelling of the same, may be named cer-
tain forms of degeneration which have been seen by certain investiga-
tors (Leloir, Unna, Buri) in the vicinity of the pocks, and must be more
fully described. Under the name " reticulating" degeneration, Unna
describes a peculiar degeneration of the prickle cells in which their
protoplasm, after previous swelling of the cell *in toto*, breaks up into a
reticular, fine-fibered meshwork. This degeneration is probably iden-
tical with Leloir's "altération cavitaire " ; it occurs, according to Buri,
especially in the upper region of the rete Malpighii as well as in the
central portions of the smallpox pock. It appears, according to the
recent investigators, to really participate in the development of the finest

septa in the interior of the pock, while the cell walls break down and parts of the reticulum, together with the shriveled nuclear residue, remain. Unna and Buri mention a second form of degeneration, which is called by the former the "ballooning" degeneration; it attacks, predominantly or wholly, the cells of the deeper layers (or of the pockbase), and occurs not only in variola, but also in other vesicular eruptions, as varicella and herpes zoster, being found to a far higher degree in these diseases than in variola. The cells attacked lose their prickle processes and become extremely inflated, a spacious perinuclear cavity developing in their interior; the nuclei finally swell and proliferate considerably; concerning this, it is still doubtful whether it is brought about through mitosis or through fragmentation. After the metamorphosis is completed, the degenerated cells resemble hollow sacks filled with balls (the nucleus), hence the peculiar name chosen by Unna for the whole curious process.

From the foregoing review of the more important reports of authors relative to the early changes in the epidermis in variola, the appropriateness of the remark made at the beginning is sufficiently shown—namely, that the fundamental views of competent observers on the whole process run in direct opposition to each other. There is, however, less difference of opinion in the reports upon the further course of development, reckoning from the period of suppuration of the exanthem. Here we observe a more and more abundant commingling of leucocytes (which until then had entered sparingly) with the fluid exudation in the interstices of the stroma of the pock, and with it a suppurative transformation of the lymph. These leucocytes probably originate from the blood-vessels of the papillæ of the skin involved, which latter, at the beginning of the suppurative process, as before, are distinctly swollen and increased in length, so that they project more or less from the base of the pock into its interior. At the same time, the tissue is found to be densely crowded with leucocytes which have migrated; these are found also in large numbers further up in the region of the rete, and also in the fluid exudation itself, as was mentioned above; if, then, as in the typical eruption of a variola vera, the suppuration process becomes more and more intense, in consequence of the mass-pressure of the pus formed, the papillæ of the pock-base disappear in many places, partly merely mechanically (pressure atrophy), while in part they are dissolved through the absorbent action of the puscorpuscles (abscess formation). Thus we can explain naturally the milder as well as the graver permanent results which the variolous process so frequently leaves in the skin, and which have been minutely

described in an earlier part of this work. (See "Variola vera" and "Variola confluens.")

The regional confluence of the single pocks (or individual pocks) in cases of variola confluens is, as has been indicated in the proper place, a consequence of the breaking down of the tissue walls separating these pocks. These boundaries are, however, to speak more exactly, always represented at first, even in the immediately contiguous pocks, by a wall of proliferated epidermal cells in the border zone; even when the neighboring cell walls are in immediate contact, confluence does not necessarily follow. It is quite clear that confluence first occurs when this boundary wall is broken down, which may quite easily happen in cases of special vehemence of the suppurative process. The rupture finally occurs partly by mechanical force on the part of the crowding mass of pus, and partly by absorption on the part of the aggressive pus-corpuscles; neither of these processes probably needs further detailed description at this point.

The hemorrhagic pocks in variola pustulosa hæmorrhagica are not, in their anatomic relations, essentially different from those of the ordinary variola; they are distinguished from the latter mainly by the fact that blood is more or less plentifully mingled with their contents (E. Wagner). According to the stage of the disease and the time of death, in the investigation of individual pocks we of course find the stages of development more or less advanced. The simple petechiæ and ecchymoses, which, in the form of variola mentioned (variola pustulosa hæmorrhagica), are met with in greater or smaller numbers on the skin, together with the hemorrhagic pustules, correspond to smaller or larger capillary extravasations of blood, which have taken place into the pars reticularis corii and more rarely extend into the papillary layer. In the primarily hemorrhagic form of smallpox (purpura variolosa) real smallpox pocks are in most cases entirely wanting; the blood extravasations mentioned reach, on the other hand, their greatest number and size. The exuded blood in these cases usually infiltrates all the layers of the skin more uniformly, and often appears at the affected part as an abundant extravasation in the subcutaneous connective tissue.

The retrogressive and reparative changes during the period of recovery need only a few explanatory remarks. The drying up of the pus, in pocks which have remained uninjured, begins, for reasons which are easily comprehended, in the center and in the region bordering on the horny layer which covers the pock, and spreads from this outward toward the periphery and down toward the base of the pock. Inde-

pendently of this, the new formation of epidermis begins from the edge, so that the newly formed epidermis, advancing gradually toward the center, extrudes from below the drying-up pus deposits found above it. Thus finally originate those lentil-like forms which, lying in the epidermis, are thrust off spontaneously or may be removed artificially at the proper time, and which present, on account of the thickness of the epidermis, so important an appearance on the palms of the hands and the soles of the feet. (See the earlier account.)

If the removal of these forms takes place prematurely, then we naturally see, in the central region of the former pock, a moist spot, denuded of epidermis, which either is subsequently covered with skin or is closed by the formation of scar tissue.

The histologic relations of the pocks in the mucous membranes have been only very imperfectly studied. That they, in their time of development, are somewhat in advance of the neighboring skin pocks has been already mentioned, and the fact is explained by the more delicate texture of the mucosa. It is probable that essentially similar fundamental processes occur in these as in the skin-pocks, and that presumably only differences in degree exist. Concerning the diffuse and non-specific changes in the mucous membranes, more exact data will be given in the following section, under the heading of Postmortem Findings.

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POSTMORTEM FINDINGS.

Bodies of smallpox patients usually show only slight rigor mortis, and a condition of nourishment varying with the stage of the disease and the previous condition of the individual. There are generally large areas of hypostatic congestion; bedsores are often present (see earlier).

On the skin we usually find, in the ordinary forms of smallpox, the pustular pocks arising from the exanthem, as well as some remains of the same (crusts, excoriations, and ulcerations). The congestive hyperemia which was present during life in the neighborhood of the pustules seems, naturally, to have disappeared at death, and the skin is correspondingly decolorized. Therefore in the hemorrhagic cases the patches originating from the extravasation (ecchymoses and petechiæ), as well as the hemorrhagic pustules with their peculiar coloring, stand out so much the more distinctly on the pale surface of the body. Nearly always one meets in the neighborhood of the mouth, nose, and throat characteristic pustules or corresponding defects of the mucous membrane (ulcers, which are small or which, through confluence, have become larger).

But also further down, in the upper part of the esophagus, in the larynx, in both bronchi, and, indeed, in the bronchial tubes of the second and third order, one has frequent opportunity, in the (severe) cases of variola which come under postmortem examination, to assure one's self of the presence of characteristic pustules and smallpox ulcers. In the mucous membrane, at the point of bifurcation of the trachea, the larger ulcerative losses of substance (which have resulted from confluence) show themselves with the greatest relative frequency. In the hemorrhagic cases, finally, the mucous membranes of the upper passages are, like the external skin, more or less richly beset with blood extravasations.

Besides the above-mentioned specific signs of the pathologic process, distinct traces of a more diffuse affection of the mucous membranes are usually not lacking, which latter, on investigation and consideration, appear partly as an extensive catarrhal swelling of the affected mucous membrane, partly as a considerable purulent infiltration of the tissue with local desquamation of the epithelium (in the form of larger or smaller exfoliations). In such exfoliated patches, grayish-white, greasy particles are found, lying loosely on the surface, which can be easily stripped off with the finger; under them the mucous membrane, denuded of its epithelium, appears, uninjured but unprotected. In especially severe cases, on the other hand, and especially often in the hemorrhagic cases (purpura variolosa and variola pustulosa hæmorrhagica), the above-mentioned alteration is complicated with a diphtheroid necrosis of the tissue. Such crust formations are essentially coherent; they adhere extremely firmly, and when they are separated, always leave behind distinct, deeply penetrating gaps in the surface. Catarrhal swellings and purulent infiltration are met with moreover, as a rule, in many regions

in which no smallpox pocks usually occur; as, for example, in the region of the Eustachian tube, of the middle ear, in the nasal duct, in the more distal portions of the esophagus, and in the deeper and finer divisions of the bronchial tree.

In addition to the signs of a terminal edema, hypostatic changes in the lungs are quite usual. For the greater part we find simple splenization (hypostatic hyperemia and extensive collapse of the lungs), but we may find also lobular pneumonic thickenings of a catarrhal, croupous, or mixed nature. Lobar pneumonia and abscess of the lungs are decidedly rare occurrences.

The heart, in those cases in which death occurred during suppuration or even later, is usually relaxed and soft, the muscle appears of a dirty color; the microscopic examination shows, as a rule, disintegration of the fibers, besides some fatty degeneration (formation of the finest granules). The liver, like the heart, shows, under these circumstances, the phenomena of parenchymatous degeneration, and is accordingly somewhat enlarged and soft. On section it appears turbid; the contour of the liver lobules is indistinct or obliterated.

In individual cases in which the degenerative process has advanced further, we have a picture which resembles an acute phosphorus-poisoning; that is, we find a marked fatty degeneration. A large amount of thin, bright-colored bile is generally present in the gall-bladder. The spleen presents the characteristics of an acute splenic tumor; it is enlarged to a variable extent, its capsule is tense and shining. The pulp is soft in consistency, almost liquefied; its color is reddish-gray; the Malpighian bodies are generally not to be seen. In the kidneys, lastly, we find the well-known picture of a parenchymatous disease; to describe it more in detail, we find swelling, a cloudy appearance, and a more or less yellowish color (fatty degeneration of the epithelium). All these findings are noted especially in the pustular forms of variola (including also variola pustulosa hæmorrhagica in the most fatal cases), and especially when death occurs, as it usually does in the pustular forms, during the period of suppuration or of commencing desiccation.

An exception may be noted in all those fatal cases that come to be examined after death which has resulted from events and complications which appear late, even after the maximal point of the disease is passed. Here probably compensatory processes have already taken place, and, corresponding to these, under such peculiar circumstances, heart muscle, liver, spleen, and kidneys have somewhat resumed their normal appearance. But the spleen, in these rare cases, is usually somewhat

diminished in size and its capsule is wrinkled.   On the other hand, we observe that the parenchymatous changes are lacking or but slightly developed, even when death occurs at the beginning of suppuration (Curschmann).

A quite exceptional position is occupied by the cases of purpura variolosa in which (compare the earlier account) death in the first days of the disease is the absolute rule.

Here, as has been recently determined with tolerable certainty (Ponfick, Golgi, Curschmann), the parenchymatous changes are, as a rule, entirely lacking.   The organs named, therefore, show at the autopsy a condition entirely different from that described above.   The heart muscle in purpura is firm and brownish-red in color ; the organ appears closely contracted in death and not dilated.   The liver is not enlarged and is also firm ; on section, it appears rich in blood and the boundaries of the lobules are distinct.   The spleen is small and hard, its cut surface is dark brownish-red with sharply distinguishable Malpighian corpuscles.   The kidney also appears of normal size, of normal consistence, and its parenchyma is of normal appearance.   But in these cases we find in the mucous membrane of the pelvis of the kidney, of the ureters, bladder, etc., more or less numerous interstitial and free hemorrhages (Unruh).

From all reports on this subject it follows that the above-mentioned parenchymatous degenerations of the organs are really prerogatives of the suppuration process, and not consequences of the specific variolous affection.   They occur in variola only when the (very frequent) secondary infection of the organism with pyogenic cocci, which is the cause of the suppuration, has played a considerable and important part in the development of the pathologic process.

It is quite different, on the other hand, with another change occurring locally, which Weigert has described in the liver, spleen, kidneys, and lymph-glands in the early stages of suppuration of pustular cases, and also in a single case of hemorrhagic variola.   It appears to stand in direct causal relation to the specific variolous infection.   The specific cells of the organ are found in quite circumscribed areas dissolved and degenerated into clod-like masses, while the neighboring cells, the outlines of which are still distinctly recognizable, appear non-nucleated and opaque.   The similarity of the smallest degeneration foci to primary changes in the skin pocks at once attracts attention ; therefore Weigert is inclined to see in it an analogue of the skin exanthem.

The blood found in the chambers of the heart after death from variola is generally dark colored, usually fluid or only slightly coagulated,

with a small amount of fibrin. The blood in other parts of the body shows the same peculiarity.

The mucous membrane of the stomach and intestine is in general free from pocks or their results. An exception to this rule is presented by the lowest part of the rectal mucous membrane, in which, as in the vulva and introitus vaginæ in women, pocks and pock ulcerations are not infrequently found. Moreover, the changes in the stomach and intestine are limited to catarrh and, in the hemorrhagic cases, to blood extravasations. The latter usually occur abundantly in the stomach, while in the intestine they are more plentiful in the jejunum and colon, the ileum either remaining free or being only slightly affected. The extravasations in the stomach and intestine are partly interstitial and partly free ; the free extravasations usually appear dark in color. In certain cases of ordinary (pustular) variola, increase in size of the intestinal follicles, with corresponding enlargement of the mesenteric glands, is found at the autopsy.

In hemorrhagic variola, and especially in purpura, more abundant blood extravasations occur, not only in the places above mentioned, but also in many other parts. They are, as a rule, lacking in such cases in the heart muscle, in the liver, in the spleen, and in the substance of the kidney, also in the brain and spinal cord, while they are more or less frequently found in greater or smaller numbers in nearly all other parts of the body. These signs of the hemorrhagic diathesis are in form partly hemorrhagic infiltrations of the tissue, partly superficial hemorrhages ; they may be hemorrhagic inflammatory exudates or they may be a combination of all these forms, especially the mixed forms of interstitial and superficial simple extravasation. Among the other localizations of the hemorrhagic diathesis which have not yet been mentioned, but which deserve mention, are the following : the serous membranes, the loose connective tissue of the body, the voluntary muscles, the joints, and the bone-marrow. Of the serous membranes, we find the pleuræ and pericardium most frequently the seat of hemorrhage, but the peritoneum not so frequently. In the subcutaneous connective tissue, in the anterior and posterior mediastina, and in the retroperitoneal connective tissue, multiple extravasations are quite usual, especially in purpura. In the cellular tissue of the pelvis of the kidney and its capsula adiposa, these extravasations usually become especially large, so that they have, certainly not without reason, been made in part responsible for the extremely intense lumbar and sacral pain experienced in these cases. In the voluntary muscles hemorrhagic foci occur more frequently ; in the joints, especially the knee-joint, besides the frequent

hemorrhages into the synoviæ, true hemorrhagic extravasations have at times been met (Curschmann). Hemorrhages into the Graafian follicles of the ovary are very frequent, and are quite the rule in the mucous membrane of the Fallopian tube and the uterus; on the other hand, hemorrhagic areas in the stroma of the ovary, as well as in the region of the testis, may be counted among the decidedly rare occurrences. In bone-marrow we find in purpura variolosa, without exception, hemorrhages of great number and extent. In the affected regions the marrow appears changed to a dark red, nearly fluid mass, within which there are scarcely any marrow cells, red blood-corpuscles being almost the only cells found. An essentially different condition is shown by the bone-marrow in the purulent stage of the ordinary and confluent forms of variola. Changes occur here which are quite analogous to those seen in the spleen in these cases (Golgi); that is, more or less hyperplasia is present. In consequence of this, the matter appears grayish-red in color, very soft in consistency, and markedly increased in volume, while the microscopic examination reveals a surprising increase in the number of giant-cells and of white marrow-cells, together with fewer red-colored hematoblasts. While the change just described is diffuse in its nature, Chiari has recently discovered another alteration in the bone-marrow of those who have died of smallpox; this change occurred in multiple small areas, hence is disseminated, and is more accurately described as "osteomyelitis variolosa." This alteration is found in variola, according to the above-named author, with surprising frequency (in 72 % of all the cases investigated by him); the affection seems to be widely distributed over the bone-marrow. Its beginnings may be distinctly recognized in the eruptive period of the disease, while its remains may be seen for a considerable time after the disease in the corresponding regions has run its course. Osteomyelitis variolosa manifests itself in the form of small foci from the size of a poppy seed to half the size of a pea, whitish, grayish, or yellowish in color, and often surrounded by a reddish areola. They consist principally of large, polyhedral, flattened (epithelioid) cells which have probably resulted from a pathologic change in the marrow cells; these, although nucleated at first, later appear to be without a distinct nucleus. Besides, there are found in the osteomyelitic foci a few leucocytes, together with traces of an exudation which is coagulated in filaments, and hence is probably fibrinous. The areas of osteomyelitis variolosa end in an early necrosis, which advances from the center to the periphery, as is undoubtedly shown by sections from different portions of the diseased mass; on the other hand, suppuration of the diseased focus does not occur. On

account of the very great frequency of its occurrence, because of its appearance in the early stages of variola, and, finally, because of its peculiar pathologic behavior, which reminds us of that of the primary variolous changes in the skin, Chiari believes that we must see in this variolous osteomyelitis a specific product of the smallpox virus, and we cannot deny that there is a certain justification for this idea. Further investigations must teach us more about this subject, and in reference to all the histologic peculiarities we must here refer directly to the original work. With regard to the clinico-symptomatologic relations we may note here that Chiari is inclined to bring the severe pains in the limbs which occur in the initial stage of many cases of variola into causal relationship with the development of this specific osteomyelitis.

A pathologic change essentially similar to the affection described occurs also in the testes (orchitis variolosa). The specific variolous inflammation of the testes seems to be extraordinarily frequent, or at least it is frequently found in the autopsies of many smallpox cases (Chiari). Here also we find the change occurring in small, disseminated foci; it is recognizable in the early period of the disease, and reaches the maximum of its development during the suppurative stage; after previously undergoing necrosis of the pathologic products, it heals, leaving behind small scars in the testicular substance.

The foci of orchitis variolosa have their seat pre-eminently in the interstitial substance, from which, however, they may attack the seminal tubules. Their size varies from that of a pin-head to that of the foci found in the bone-marrow. They consist chiefly of a small-celled infiltration of the tissues, which is permeated and surrounded by a finely fibrillar or finely granular exudation. In the necrobiosis which begins early and radiates from the center of the focus toward its periphery, in addition to the infiltrating round cells, the pre-existent cells of the interstitial tissue as well as the epithelial cells of the seminal tubules are destroyed, and in this way defects of substance result, which are later replaced by the formation of scar tissue. The orchitis variolosa is frequently accompanied by diffuse swelling of the testes; no trace of suppuration is, however, found, just as in the variolous osteomyelitis and as in the peculiar necrobiotic foci in the liver, spleen, kidneys, and lymph glands, described by Weigert (see above), and characterized by him as the pock-like forms in the parenchymatous organs.

After Beraud, Trousseau, and the author had earlier called attention to the frequent occurrence of inflammation of the testes in variola, orchitis variolosa more recently became, as above stated, the object of

careful investigations by Chiari. The pathology of variola owes to him especially the knowledge of its more exact histologic relations, as well as an attempt at a theoretic explanation. The investigations made in Basle of late years are such as confirm, on the whole, the views advanced by Chiari (Roth); the theoretic conclusions naturally, however, need further discussion.

In the foregoing review of the postmortem findings, we have had it in view to give only the more usual and those which occur with the greatest regularity. Everything else is omitted which occurs more or less frequently in complicated cases of smallpox with fatal termination. Under the last heading we might repeat all that has been said earlier concerning the occurrence of phlegmonous inflammations, abscesses, and purulent exudations in the region of the tongue, of the throat, and of the larynx, in the loose connective-tissue layers of the body, in the pleuræ and in the pericardium, in the muscles and joint cavities, etc.

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DIAGNOSIS.

THE diagnosis of smallpox may be extraordinarily easy, or under certain circumstances very difficult, or even at times impossible. The former statement is true in well-formed and in well-developed cases in the period of eruption, and still more in the period of suppuration; the latter statement is true of the initial stage, sometimes also of the period of eruption as well as of irregular and undeveloped types of the disease. The especially important points for diagnosis are the epidemic relations and also certain clinical peculiarities which occur especially in variola.

During the prevalence of a smallpox epidemic one is in general compelled to regard as suspicious any case which sets in acutely with high fever, especially when it can be shown that the patient has had any communication, direct or indirect, with a smallpox patient, and when personal susceptibility can be presupposed. The latter may be assumed if the patient has not been inoculated or if too long a time has elapsed since vaccination or revaccination (see for particulars under " Vaccination "). In such cases also the initial fever, especially in cases of later varioloid, is often very light and the history is indefinite and misleading, so that it is not to be wondered at that erroneous conjectures as to the nature of a doubtful case are by no means seldom made, up to the time of the critical moment of the eruption (that is, in general up to the fourth day). Thus the first cases of a smallpox epidemic, in the absence of more particular diagnostic points, often pass without an early diagnosis, whether they set in with mild or severe symptoms. It is naturally very easily possible to confuse the early stages of smallpox with such other acute febrile diseases as begin with a sudden rise of temperature and with intense general symptoms. Among these we may place pneumonia and influenza; of the acute exanthematous diseases, scarlet fever and typhus exanthematicus, as well as relapsing fever and, less frequently, measles and typhoid fever. Of especial value for the early diagnosis of smallpox are certain local signs which frequently appear in variola especially in this period of the disease. In this connection we may mention first the lumbar and sacral pain, as it very decidedly plays a frequent and important part among the subjective symptoms of the initial stage of variola, while in none of the other diseases named

(unless we except influenza) does it occur so severely, if at all. In the second place, we should mention the initial exanthems, which were described earlier; among these, the so-called scarlatinous exanthem— correctly called the hemorrhagic erythema in the femoral triangle (or shoulder triangle)—especially possesses an absolutely pathognomonic importance, as it in general occurs in no other disease except variola. Were this symptom frequent or quite constant, instead of being, on the contrary, very rare, then the diagnosis of the initial variola would possess not the slightest difficulty, especially as this symptom nearly always develops very early or even at times is the first of all to show itself (W. Bernouilli, Curschmann). Little diagnostic importance can be ascribed to the severe pain in the head, the dizziness or benumbing of the sensorium, and delirium, as all these and similar cerebral symptoms occur very frequently in other acute infectious disease and toxemic conditions.

A positive opinion as to whether the disease is smallpox is usually not possible until that phase of the disease is reached in which, if infection with variola has occurred, the typical exanthem usually breaks out; that is to say, near or after the end of the third day of the disease (see above). If at this time there is no eruption, in spite of all expectation, then we have to think of variola sine exanthemate, if the fever falls abruptly and definitely, if a condition of well-being is resumed, and if the assumption of a smallpox infection is sufficiently supported from epidemiologic considerations and the history of the case. Such cases may, in general at least, be unhesitatingly attributed to the prevailing epidemic, and are naturally also correspondingly valuable from a statistical standpoint.

As in that fortunately rare form of smallpox, purpura variolosa, the peculiar, universal hemorrhagic erythema develops without exception within the first three days of the disease, this condition involves at the same time the possibility of an early diagnosis of these cases, if our experience is sufficient. Above all, the epidemic conditions existing at the time are determining factors in the diagnosis, as well as especially the etiologic relations of purpura with other undoubted cases of smallpox. Besides these, other diagnostic points should be considered : namely, that certain initial symptoms of variola, as the lumbar and sacral pain, regularly reach, in this form of variola, a very unusual intensity, and may even be distinctly felt by the patient toward the end of the period of incubation.

In the period of eruption smallpox and measles are more frequently confounded, and this explains the historic fact, which at first sight seemed

so surprising, that in former times these two diseases were very frequently regarded as one (compare History). The reason for this error is that at the time of eruption the exanthem of smallpox is papular in its nature, and this to a certain extent resembles the papular exanthem of measles. The main difference between the two exanthems consists in the fact that the exanthem of measles remains papular, while that of small-pox soon becomes vesicular, and later pustular. But, in addition to this, the papules of measles have, even from the beginning, the tendency to occur together and to arrange themselves in groups (or corymbose *) ; that is, with alternating paler interspaces. This is not the case in small-pox, and it is this which gives to the skin the measly appearance peculiar to measles. On the other hand, the general differences between the two diseases are almost more important than the cutaneous differ-ences, and they should therefore be taken into especial account in the dif-ferential diagnosis of the two in the critical stage (without regard to the epidemiologic factors). Usually several [four] days of severe catarrhal symptoms on the part of the conjunctiva, the nasal mucous membrane, and the whole respiratory tract precede the outbreak of the exanthem in measles, while such a catarrh is present to a very slight degree in variola at this time. But the behavior of the fever is the most different of all ; in measles, before the outbreak of the exanthem, the fever is slight, but usually rises considerably with the eruption, while in variola, on the other hand, the fever is usually high in the initial stage, but regularly falls more or less with the eruption, even in the severe cases. This peculiar defervescence is in general most sharply characteristic of variola as com-pared with all the other exanthematous diseases (scarlet fever and exan-thematic typhus), and especially when compared with varicella, which, on account of the vesicular form of its exanthem, quite vividly reminds one of the real smallpox during the period of full development. As the nosologic unity of smallpox and varicella has been asserted and pro-claimed with all possible positiveness by many, and even by very prom-inent investigators (F. von Hebra), this seems the proper time to enter somewhat into detail for a moment on this much-discussed question of the identity or non-identity of the two pathologic processes. Regarded in the right light, this hypothetic identity of variola and varicella depends on a very external and a very transient similarity, which con-sists in the fact that in both these acute infectious diseases, vesicles develop at a certain time in the skin ; that is, fluid is exuded in certain foci between the cutis and the epidermis. Yet there are important differences, also purely morphologic, between the two kinds of efflores-

* From κόρυμβος, a cluster of fruit or a bouquet of flowers.

cences. The efflorescence in variola passes regularly through a pap-
ular stage before the pock vesicle appears on the fully developed
papule. In varicella, on the other hand, the vesicles appear forthwith
on smaller or larger quickly forming reddish spots, or macules, without
the development of papules. For this latter reason, the full development
of the single pock in varicella takes place far more rapidly than in
variola, usually requiring less than a whole day, so that on the second
day of the disease the maximal development of the individual vesicle
is usually already past. Also the vesicles in the stage of full develop-
ment present a different appearance in the two exanthems, due to a dif-
ferent condition of the epidermis. The epidermal covering of the ves-
icle of varicella is very thin, so that the fluid contents, during the short
period of full development, show through very clearly; in the vesicle
of variola, on the other hand, a quite thick epidermal covering lends to
the surface of the pock a peculiar luster, like mother-of-pearl, and,
united with it, a certain degree of translucency. Finally, the involu-
tion of the pock of varicella takes place very quickly, since the vesicles,
when scarcely developed and after their contents have become somewhat
turbid, already begin to dry and to change into small, brownish, trans-
parent crusts. In variola, on the other hand, the period of full develop-
ment, after lasting for several days, is followed by the purulent change
of the fluid contents of the vesicle before, much later, involution (or
desiccation) begins.

In addition to the above-mentioned morphologic criteria, which in
themselves are quite sufficient to show with probability the specific nature
of varicella as opposed to variola, other criteria, based on the general
clinical course, and also on the etiology, might be given. Of the course,
the following may in particular be emphasized : In contrast to variola,
a specific initial stage is lacking in varicella or, even in the best-marked
cases, is so short that, in spite of it, the exanthem breaks out after a few
hours. The eruption itself is frequently accompanied by a considerable
elevation of temperature and not by a decline, and it is usually quite
general at once ; yet after-crops appear quite frequently in the following
days, and are then marked by slight, renewed elevations of temperature.
From what has been said, this much certainly follows, that the patho-
logic events in varicella are quite different from those in variola, and
that therefore these two processes are presumably different.

But, finally, also etiologic differences abound which show directly
that the diseases in question belong to two different species. It has
been known for a long time that epidemics of both kinds (variola and
varicella) sometimes indeed coincide for a certain period, and so natur-

ally get mixed up with each other. Nevertheless they much oftener prevail at times perfectly separate and distinct from each other. It is further known that the conspicuous prophylactic against variola—namely, vaccination—has no influence at all against varicella, and, finally, it is certain that variola and varicella assure no immunity for the future against each other. For all these reasons, morphologic, clinical, and etiologic, the duality of the two diseases is proved by overwhelming evidence, and therefore it is most desirable that we should in a given case be able promptly and correctly to determine the differential diagnosis beween the two. The points named above assure this possibility quite sufficiently for most cases.

Failure to see the exanthem after it is developed can occur only in those very light cases of varioloid in which the number of pocks is very small and the pocks are very widely scattered and perhaps in inaccessible places. One should never delay therefore when, for other reasons, there is any suspicion of smallpox, in which it is of such vital importance to make a correct and early diagnosis; he should at once inspect carefully the whole surface of the body of the patient, and in the examination he should not neglect the accessible mucous membranes of the mouth and throat. It happens at times that one discovers at once on these one or the other characteristic variolous pocks when he experiences trouble in seeing, over by far the greater part of the surface of the body, the extremely few and but rudimentarily developed pocks.

Against a confusion of variola with impetigo, acne, pustular syphilides, etc., we guard ourselves by proper inquiries regarding the time and circumstances under which a questionable eruption appeared. The morphologic characters of the true variola pocks are characteristic; peculiar to variola alone, as has been sufficiently shown in the preceding account. It is, therefore, not to be feared that mistakes of the kind just mentioned will often happen to one after he has had a little practice.

LITERATURE.

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PROGNOSIS.

THE question concerning the prognosis of variola cannot be answered in a simple and concise form, as the question itself is a complicated one and its answer still more so. As a preliminary explanation of this fact, we may quote the very general remark that smallpox is extremely variable in malignancy, and hence the prognosis will show correspondingly great variations.

Considered now in detail, we are concerned first with the prognosis of variola on the whole and in general, and for this the observations relating to it, historic as well as actual, must be outlined and also afterward discussed more in detail. In the second place, we are concerned with the prognosis of each separate case (or with the individual character of the disease); that is, with the enumeration of all those clinical elements or factors which, according to experience, are capable of producing approximately a more favorable or more unfavorable course in a given case. First of all, as concerns the general prognosis of variola, the historic fact is firmly established that in former centuries smallpox contributed on the average far more than it does now to the general mortality. While, for instance, in the eighteenth century it is calculated that in central Europe about a tenth (7 to 12 %) of all deaths were, on the whole, attributed to smallpox, the mortality at the present time from smallpox scarcely reaches on the average a tenth part of what it was then; that is, it is not quite 1 %. This depends partly on the fact that in the nineteenth century the smallpox epidemics and pandemics have been on the whole much less frequent and less extensive than formerly, and partly on the fact that smallpox has become less malignant; that is, that it claims, on the average, fewer victims. This general difference in the morbidity and mortality of smallpox coincides historically very exactly with the general introduction of vaccination, accidentally also with the turn of the century, as Jenner's publications appeared about 1800 A. D. and vaccination was, in great measure, immediately introduced. Furthermore, this change relates exclusively to those portions of the European continent in which vaccination and, later, revaccination found general acceptance. The probable conclusion is therefore fully justifiable that the reduction in the general malignancy of variola is to be ascribed pre-eminently to vaccination and revaccination. (See the later section on "Vaccination" for further particulars.)

It follows, further, for the general prognosis of variola at the present time, that though now and then a smallpox epidemic occurs in lands where vaccination is practised, and though it continues to develop, yet a smaller mortality from it is to be anticipated.

This presumption has been so far verified that its correctness can no longer be doubted. In addition to this, it has been shown that in large mixed communities the smallpox, in its epidemic spread, not only attacks, as a rule, a far greater percentage of the unvaccinated and poorly revaccinated, but is far more fatal to these, or at least the attack is far more severe. Accordingly it may be said in general that at the present time the prognosis in variola is in great part dependent on vaccination and revaccination ; that is, that the average malignancy of the disease, and at the same time the number of cases, is in general in inverse ratio to the strict enforcement of those prophylactic measures. (See for further details under " Vaccination.")

Aside from these conditions which have been mentioned, and which are probably in direct causal relation with protection by inoculation and by revaccination, at the present time a quite recognizable influence on the prognosis is also exerted by the so-called *genius epidemicus.* It cannot be denied, and it would be doing violence to the facts submitted to deny, that even now many smallpox epidemics, under otherwise similar conditions, show a more malignant character than others. We should in these cases think of transitory variations in the malignancy of the cause of the disease, perhaps also of variations in the natural susceptibility to the disease, or perhaps of both together. Likewise, in making his prognosis, one does well to take into consideration the character of the prevailing epidemic.

Of real importance for the prognosis in general is the clinical form of the disease, in which connection the different modifications of smallpox, which are known under the names variola vera, variola confluens, varioloid, etc., differ very considerably from each other. The first place in malignancy is taken without doubt by purpura variolosa (the primarily hemorrhagic form of the affection), from which recoveries have [seldom or] never been observed ; next to this stands variola pustulosa hæmorrhagica, the fully developed cases of which (compare the earlier description) almost always prove fatal. The mortality is very great for variola confluens also, reaching at least 60 % of the cases. On the other hand, we can say that varioloid and variola sine exanthemate only rarely prove fatal, and then only under exceptionally unfavorable individual circumstances (for further particulars see below). Complications also occur only exceptionally in these forms of the affection.

The widest scope for the settlement of the prognosis is no doubt afforded by the regular form of variola, known as variola vera discreta ; we include under this term all those cases which, without being confluent to any considerable extent, or without entirely degenerating into hemorrhagic cases, yet show, after the appearance of the exanthem and during its suppuration stage, a decided suppurative fever with severe local and general concomitant symptoms.   In all the cases belonging to this class the so-called *genius epidemicus*, and also the individual elements, are equally concerned in making the prognosis more favorable or more unfavorable, and in increasing or decreasing the number of fatal cases reported in the " bills of mortality."   The average number, based on the general statistics of smallpox, of those who die of variola vera discreta may be placed at about 25 %, yet it is greater than this in many of the severe epidemics ; thus, in the epidemic of 1870 to 1872, the number was considerably higher (30 to 40 %, according to Curschmann).

As concerns the complicated cases of smallpox, it is in the nature of things that, in general, the prognosis of the case is influenced unfavorably by every complication of any importance which occurs during its course.   If, therefore, in certain epidemics complications of a certain kind occur more frequently, or if, in general, complications appear frequently, then the epidemic results, as a rule, unfavorably.

Among the individual factors which have an important bearing on prognosis may be mentioned especially age, sex, constitution, and the general previous health of the patient.   Of all periods of life, childhood, before the introduction of vaccination, was especially endangered, as not only the number of children attacked in each new epidemic was disproportionately large, but also the severer forms, variola vera and variola confluens, occurred disproportionately often in this first decade of life.   This proposition applies even at the present day to those children who have not been vaccinated ; apart from these, however, in children who have been successfully vaccinated smallpox is scarcely ever observed at this age.   In advanced age—that is, at fifty years or upward, as well as in the early period of life—smallpox is in general a very dangerous disease, and it is dangerous at this time even when it is not itself of an especially severe form.   That older people exhibit a lessened tolerance for acute febrile diseases of every kind—pneumonia, influenza, typhus, etc.—is a well-established fact, and need not therefore be especially surprising in the case of variola.   With regard to sex, it may be stated that variola is particularly fatal to women in the pregnant or puerperal condition, and the death-rate among them is therefore very

high; among many reasons which might be given for this fact, one of the most important is that under these circumstances the disease readily assumes a hemorrhagic character (variola pustulosa hæmorrhagica). The same is true for inebriates and for debilitated individuals of both sexes, as has been mentioned and explained more in detail in an earlier portion of this work. Finally, convalescents from other acute diseases (typhus, pneumonia, etc.) not only easily acquire variola if exposed to the infection, but usually show little tolerance for it. From all that has been said it follows that the personal circumstances of the patient are very important in various ways for the prognosis of variola in individual cases, and they may at times be determining factors.

Finally, I will here give a brief summary of the symptoms and peculiarities of variola which have a favorable or an unfavorable bearing on the further course of events in the individual case. In this respect the following may be stated, or rather, by way of reference, simply repeated :

1. A remarkably short stage of incubation appears to occur especially in purpura variolosa (Zuelzer), and therefore indicates a bad prognosis.

2. A mild initial stage precedes, especially, only the mild cases of variola (varioloid) ; it therefore indicates a favorable prognosis.

3. A severe initial stage gives no certain indication as to the further course of the disease, as it is observed in mild as well as in severe cases of the affection.

4. Unusual intensity of the lumbar and sacral pains makes us fear hemorrhagic smallpox, especially when these symptoms are already present in the prodromal stage.

5. A distinct enlargement of the spleen in the initial stage is generally found only in severe cases of smallpox (variola vera, etc.), not in mild cases (Curschmann).

6. Of the two forms of initial exanthem, that resembling measles occurs more frequently in varioloid, while the scarlatinous form belongs rather to the severe cases. The former is therefore a rather favorable sign, while the latter is unfavorable.

7. A universal scarlatinal and at the same time hemorrhagic erythema on the second day of the disease permits, at a time when smallpox is prevalent, the assumption that it is a case of purpura variolosa and has therefore a fatal significance. This assumption is still further supported by the appearance of other signs of the hemorrhagic diathesis.

8. A prompt decline of the fever, with the beginning of the eruption of the smallpox exanthem, is the surest sign of a mild case of

variola, and is therefore an extremely favorable prognostic indication.

9. A delayed and imperfect decline of the fever in the period of eruption indicates a severe type of variola.

10. A slow and at the same time typical outbreak of the exanthem is peculiar to variola vera. A precipitated and more or less atypical eruption is found, on the one hand, in varioloid; as well as, on the other hand, in variola confluens. The decision as to which type is before us depends in part upon the extremely important and very different conditions of temperature in the initial stage, and in part upon the number and the arrangement of the pocks.

11. Another and higher elevation of temperature toward the end of the period of full development of the rash, but especially a continuous febrile condition, occurs in the severe and especially in the very severe forms of smallpox (variola vera and variola confluens), and should serve as a warning concerning the further prognosis.

12. A continuous afebrile state, following the period of eruption and full development, as well as early signs of desiccation, indicate, on the other hand, a mild form of the disease (varioloid), and the prognosis should therefore be favorable.

13. The danger of the period of suppuration stands in direct relation to the number of suppurating pocks which are present, to the intensity of the concurrent inflammatory symptoms connected with the skin and mucous membranes, and to the intensity of the fever (as well as of the other general symptoms).

14. Some confluence of the pocks in the stage of suppuration is to be expected when they cover considerable areas in their development.

15. The same is true to a still greater degree of the hemorrhagic change of the smallpox exanthem and of the other signs of a secondary hemorrhagic diathesis.

16. Hyperpyretic elevations of temperature during suppuration forebode a phenomenon occurring in the death agony, and the same is true of the less frequent collapse of the temperature.

17. In cases of severe smallpox (variola vera, etc.) the sooner the fever during the period of suppuration shows a tendency to fall again and prepares to decline, the less do we need to fear serious complications in the further course of the attack.

18. The distinct abatement of the local symptoms in the skin and mucous membranes has a prognostic value similar to that of the abatement of the suppuration fever.

19. Complications have a prognostic value proportioned to their clinical importance (previously innate in them).

In the foregoing review I have enumerated and recapitulated the most important points which, on the side of the special symptomatology and course of the disease, may be advanced for the prognosis of small-pox in individual cases.

TREATMENT.

GENERAL PROPHYLAXIS.

VARIOLA is justly known as the protagonist among the infectious diseases ; its prophylaxis therefore demands the enforcement of the two chief rules which are based on the principle of preventing the removal of a pathogenic germ to another place and the transmission of that germ to another susceptible individual. These two prophylactic measures are called, in general, isolation and disinfection. In the great transmissibility of the smallpox germ (volatility of the contagium), and in the no less great vitality of the same, it seems especially necessary, so far as variola is concerned, to enforce the rules just mentioned with all possible strictness, and so much the more as the disease, more frightful than almost any other, is also, in its worse forms, dangerous to life.

This care would, nevertheless, be superfluous if the natural susceptibility to the disease were not present, and if it were not so great and so extremely general. An annihilation of the susceptibility therefore forms the other, still more important, because more radical prophylactic measure. Now, the human race possesses in vaccination and revaccination a means of destroying the predisposition to the disease again and again which is not equaled in the whole history of prophylactic medicines. As, however, unfortunately the custom of enforcing these incomparable rules has not yet been made obligatory, and as we have to contend with ignorance and folly in many places, isolation and disinfection still most certainly possess their very real importance.

Separation (or isolation), as the word itself explains, refers in the first place to those who are known to have smallpox, and, in the second place, to those who are suspected to have it. This latter desideratum is justifiable, at least when the possibility of its being smallpox is supported by other particulars ; that is, when an epidemic of variola is prevalent in the place and when the case under consideration, according to its history and earlier symptoms, has a certain appearance of being variola in the initial stage. As, moreover, a many thousandfold experience, with abundant testimony, has shown that the isolation of smallpox patients and smallpox suspects both in private and in the homes of the patients is generally not to be considered safe enough, isolation under the control of the Boards of Public Health must be

brought about, and, wherever possible, the patients should be isolated in places appointed for that purpose and away from their private dwellings. As such places cannot be provided in the ordinary wards of the public hospitals, where patients of every description have to remain, it is most necessary, in the larger places and cities, to have isolation wards in the ordinary hospitals, or, far better still, isolation hospitals established for the reception of infectious diseases and especially of smallpox cases. The former (isolation wards in the usual hospitals), so long as a small-pox epidemic has not formally declared itself in the place, may be temporarily used for the reception of the first cases until further arrangements can be made. We should also place in such isolation wards for further preliminary observation those cases which, while brought into the hospital for other reasons, showed, at the time of their reception and on investigation, symptoms which would cause us to suspect smallpox. In the special isolation hospitals, on the other hand, we should place from the beginning all smallpox patients and all persons directly suspected of having the disease during the further course of the epidemic. Moreover, it is well, and in accordance with the dictates of prudence, not to delay too long, in the beginning of the epidemic, the opening of the smallpox hospitals for the reception of patients, as the prolonged burdening of the isolation wards of an ordinary hospital with smallpox cases and smallpox suspects may, in spite of all precautions, easily cause serious consequences to the other inmates of the hospital. Sufficient room is needed for the complete separation of those cases which are known to have smallpox from those whose symptoms are at first only suspicious, as the latter should not be exposed to the former cases before the diagnosis is perfectly certain, or, in other words, before the typical exanthem of smallpox has made its appearance. For this reason, and coming within the sphere of general isolation, in the isolation wards as well as more especially in the isolation hospitals, certain portions of the buildings should be set apart for the purpose of observation of the suspicious cases, and these observation wards (it is best to have rooms with a single bed in each) should not be in too close connection with the rooms assigned to the undoubted smallpox cases.

These arrangements may appear unnecessarily elaborate, but they represent only the minimal amount of the requirements with regard to isolation which the prophylactic treatment of variola makes necessary in the rational care of the public health. For larger localities and places and those more frequently visited by epidemics they are indispensable. In Basle, for instance (with 75,000 inhabitants, and into which smallpox is frequently introduced from without), they have shown themselves just as appropriate as they are necessary, and they have therefore for a

number of years formed an integral part of the sanitary police regulations for the prevention of smallpox.

In those (ordinary) hospitals which are planned in the modern style of separate wings or pavilions, or which may be newly planned, the establishment of an isolation department with separate rooms for smallpox patients and smallpox suspects presents no noteworthy difficulties. The isolation wings should, however, be distinguished from the other wings of the general hospital by their isolated situation, and should be at least 100 meters distant from their nearest neighbors. For the hospitals built in the older style (monumental building with the corridor system), the requirement is, on the other hand, indispensable that the isolation wards shall, under no circumstances, be in the main building of the hospital, not even in a remote corner of the same, but they must always be in a separate building at least 100 meters distant from the main building. On account of the great volatility of the contagium of smallpox, the possibility of its transportation through the open air even for this distance (which also must be regarded as minimal) apparently cannot be excluded with absolute certainty. So much the more objectionable would it be to admit smallpox patients into the main building under one and the same roof with other patients.

For the special isolation hospital, the pavilion or barracks system is the only one that is suitable; for this alone makes it possible to furnish to the sick-room the air which is so essential to the well-being of the variola patient (compare later, under Treatment). But, in addition to this, the barracks system is to be recommended from an economic standpoint, because of the relative cheapness of the material which is preferably used in its construction (wood). That, besides the wards for the undoubted smallpox cases, special wards for the observation of suspected cases must be erected within the precincts of the isolation hospital may be repeated here; another and eminently important point may, however, be added: It is certainly an extraordinarily urgent sanitary desideratum, and one which should be insisted upon in the interests of the public, that, in case of a smallpox epidemic, every case of smallpox shall be compelled to enter hospital; for this purpose, proper arrangements should be made in the isolation hospital to meet the social claims of all conditions, those in better circumstances, as well as the very poor. Besides the general larger wards which contain a large number of beds, there should be, at the disposal and for the use of those who desire them, smaller rooms, with perhaps two beds in each, and also single rooms, in which wealthy patients may be lodged according to their wishes. For only in this way can we succeed, and we do in this way really suc-

ceed, in overcoming the objections which are otherwise made to the
above requirements.

The situation of the isolation hospital should be, if at all practicable,
not within the city or place, but outside and yet but a short distance
from the same ; greater distances are to be avoided, as they would cause
much difficulty in the conveyance of patients to hospital : Special means
of conveyance should always be used for carrying smallpox patients
("smallpox droskies," "smallpox litters," etc.), which should not be
used for any other purpose for the time being, and which should be
properly disinfected each time they are used. For the conveyance of
patients to hospital such persons (coachman, carriers, and companions)
should be selected as have either had smallpox or show satisfactory
evidences of successful revaccination ; besides this, after discharging
their duty, they should submit to certain measures of disinfection before
again leaving the isolation hospital (compare the description given later).
The same is true to a still greater degree of those who are entrusted with
the care and medical treatment of the smallpox patients (nurses and
physicians), and, of course, more particularly so if they do not belong to
the intern staff of the isolation hospital and have to go out and take
part outside in the affairs of men.

Finally, it is a matter of course, and involves the whole nature of
the principle of isolation, that superfluous visits to the isolation hospital,
of any kind whatever, should not be permitted ; in necessary cases the
special consent of the physician should first be secured, and afterward
the prescribed measures of disinfection should be enforced.

As regards the duration of isolation, it is to be remembered, in the
first place, that variola may be infectious in each of its stages, not
excepting the initial stage, which is accordingly to be regarded as infec-
tious. Isolation ought therefore to begin as early as possible, and should
be put into operation as often as there is well-grounded suspicion of
the occurrence of infection with smallpox ; it should begin, wherever
possible, " *ab initio morbi*," at least in the form of isolated observation
of the case. The general fulfilment of this indication is under all cir-
cumstances much to be desired, because many cases of variola, especially
those with mild initial stage, first become noticeable during the eruption or
even later, and are not until then brought under the inspection of a phy-
sician. In special cases one is often in a position, with proper knowl-
edge, to enforce early isolation with all possible energy, and isolation
should certainly begin the very moment there is no longer any reason-
able doubt as to the variolous nature of the case. As, on the other
hand, the perfectly desiccated crusts of the smallpox exanthem and the

mummies of the smallpox pustules are in an active condition to infect others, the isolation of convalescents should under all circumstances be continued as long as these persist, and should not be interrupted until the whole surface of the body is entirely freed from these exuviæ and has become definitely well. This critical point is reached in mild cases of variola considerably earlier than in the severe cases, so that naturally the duration of the period of necessary isolation must be decided each time for the individual case; it should never be wantonly shortened, nor should it be unnecessarily lengthened. It all depends on an intelligent watching of the period of healing and a most careful final inspection on the part of the skilful physician, and this should be conscientiously and carefully done in every case.

The encapsuled pock mummies in the thick epidermis of the sole of the foot usually last the longest (compare the earlier statement); this part should therefore have especially careful examination. One can easily succeed, at the right time, when they are completely hardened, in loosening, one at a time, the hardened masses which still remain in these situations, before they are spontaneously removed, and by this means the whole period of recovery may be somewhat shortened. But in no case can a convalescent from smallpox be released before the last traces of the exanthem have entirely disappeared from this region.

As the corpse of the patient who has died of variola is also highly infectious, corresponding prophylactic measures must be applied to it; early interment or cremation is to be especially recommended and protracted funeral arrangements are to be most sternly prohibited.

The other important measure of general prophylaxis against variola, which also springs from its contagiousness, is disinfection. Every thing should and must be disinfected which has been in direct or indirect contact with a smallpox patient (or corpse). In the first place, we naturally speak of the body-linen and other clothing, the bed-clothing and beds of the variola patients. The disinfection of these effects, as well as the tapestries, coverings, carpets, etc., from the private dwellings of the patient, is most surely attained by means of streams of superheated steam at high pressure in apparatus especially constructed for this purpose (vapor disinfectors or sterilizers). Apparatus of this kind are used, as is well known, in many places at public disinfection stations. They likewise belong to the most necessary requirements of a well-equipped hospital, especially of an isolation hospital, and they do the best work in every respect. Dry heat to the permissible (non-destructive) degree is less certain in its effects, and hot air is still less satisfactory. When, therefore, only the last-named simpler means of

disinfection are to be used, the articles should also be exposed for a long time (for weeks) to the air before they are used again.

For the subsequent disinfection of rooms in which smallpox patients have been kept for a longer or shorter time, we may employ fumigation with vapors of chlorin, sulphurous acid, or formaldehyd, continuing the process for at least twenty-four hours; after the fumigation, the rooms should be well aired for several days. The wall-paper should, if possible, be removed and replaced by new; if this is not possible, it should be rubbed off properly and the debris destroyed by fire; in hospitals the use of paper on the walls of sick-rooms has been rightly dispensed with.

In choosing the necessary furniture for the room of a smallpox patient, we should pay especial attention to the strength of the materials and the smoothness of the surface. The single bedstead should be of iron, and the table, chair, and other movable furniture, if of wood, should receive a coat of varnish. Curtains and carpets, upholstered chairs and sofas, because of their extreme proneness to become infectious (see Etiology), are entirely unfit for the sick-room of a smallpox patient; the same is true of decorative furniture of other kinds. For the subsequent disinfection of the furniture used, a vigorous scrubbing of the varnished surface of the walls and floors with a 5% carbolic acid solution is sufficient.

The nurses in personal attendance on the sick, and also the visiting physicians, should pay their necessary visits to the patient in special overgarments, which can be easily put on and taken off, afford proper protection to the underclothing against the entrance of the contagium, and can be disinfected each time that they are used. Very suitable for this purpose are long, buttoned overcoats or smock-frocks, reaching to the feet, consisting of thick, unbleached linen, with high collar and closely fitting wristbands, such as are rightly coming more and more into use in hospitals for the customary sick-room visits of the staff physicians. For a smallpox division, smock-frocks used only for the visits to smallpox patients should be provided in sufficient numbers, and each time after their use undergo sterilization in the steam disinfector.

Of the greatest importance, finally, is a thorough cleansing of the hands and face, the hair of the head and beard of all those who, after visiting the patient, are obliged to again come into contact with the external world. This cleansing should in general follow the ordinary rules of cleansing for operative surgery (soap and water, sublimate solution or carbolic acid solution, etc.), and therefore needs no further description in this place. The fact is that physicians have often been

the carriers of the smallpox contagion, from their previous visits to smallpox patients. They should therefore be doubly conscious of the responsibility which they, in neglecting the necessary precautionary measures, bring upon themselves under all circumstances.

Variola convalescents who are permitted to leave hospital after complete recovery need at the last a final cleansing by baths and thorough scrubbing; they should also never be allowed to leave the isolation wing until their clothing has been completely disinfected.

If we think of the minuteness of detail and expense required in carrying out all the measures which are necessary in order to perfectly accomplish the isolation and disinfection of variola cases, and if we consider that this whole complicated machinery has to be brought into requisition so frequently at the present time only because the much simpler measures of vaccination and revaccination are not always made compulsory, as they should be, then we cannot avoid a feeling of deep regret. A destruction of the natural and of the reawakened susceptibility to the disease through the individual prophylactic measures last mentioned is, and without any doubt remains, the truly rational and the safest means of protection which, up to the present time, are known, and which should therefore be brought most generally and most strenuously into use. On account of the extremely great importance of the subject, vaccination has been treated in a special section in this handbook, and we will therefore discuss it no further at this point. We have still to discuss briefly the treatment of the disease once it has broken out, or the special management of variola.

TREATMENT.

We have as yet no therapeutic agent which is a specific for smallpox at the time of the attack and when the eruption has already appeared. Attempts have been made (and quite irrational ones, too) by subsequent vaccination, or by the injection of larger amounts of the vaccine lymph, to check the progress of the disease, but they have not had the desired result. The same is true of the administration of large doses of quinin in the beginning of the disease, of enforced diaphoresis of historic memory, of the use of emetics and purgatives, and of other methods which have been tried with the object of aborting the disease. Of course we cannot say, in spite of all this, that in the future, on the basis of new observations and experiences, a specific method of treatment of smallpox may not perhaps be discovered. If, with the help of such a remedy, a genuine case of variola could be suppressed at its

onset, or if merely a presumably severe case could be changed into a light one, much would be certainly gained by such an acquisition in smallpox. Up to the present time, however, treatment must confess its utter powerlessness in both directions.

In the absence of specific agents, there remains for the treatment of variola, until something further is discovered, simply a dietetic, symptomatic method of treatment, and in regard to this, we may add the following observations : A very important desideratum is, first, a sufficient airiness and spaciousness of the place in which the patient finds himself. The urgency of this requirement increases with the number of cases collected together in a single apartment and with the severity of these cases ; for the greater the number of patients and the more intense the suppurative processes, the more easily does the air become poisoned through the decomposition of the masses of pus occurring on the surface of the body, and this may give rise to the most injurious consequences. Curschmann surely, then, did not ask too much when he demanded for every smallpox patient in a large smallpox ward, a quantity of air equal to at least 1500 cubic feet (450 cubic meters), always provided that arrangements are made for abundant ventilation either natural or artificial.

The temperature of the sick-room, as it is adapted to the febrile condition of the patients, should not be too high. It should, if possible, not exceed 14° R. (17.5° C.) (63.5° F.).

The other arrangements, especially the diet and the direct therapeutic measures, adapt themselves to the stage of the disease and the severity of the case, and, as is unavoidable, vary somewhat in different cases. For the initial stage, when there is a high fever, rest in bed and a diet suited to febrile cases are appropriate ; especially as concerns the diet, the not too sparing use of cooling and thirst-assuaging drinks. For the intense pain in the head the application of an ice-bag to the head has a soothing influence, as in other acute febrile conditions ; likewise, for the unpleasant feeling of heat in the skin, a frequently repeated bathing of the whole body with a large sponge moistened with water or dipped into a mixture of vinegar and water is serviceable. Usually we may properly disregard during the short duration of the initial fever the use of methodic antipyresis in the narrower sense of the word ; that is, by the application of cold or gradually cooled fulllength baths, as well as by the use of medicinal antipyretics (quinin, phenazone, etc.), or we may, at most, reserve such orders for the very extreme degree of heat seen in individual cases. No perceptible permanent advantage for the further course of events is produced by the

artificial production of antipyresis in the initial stage of variola, as many earlier experiences in this field of therapeutics have taught me.

If the more severe conditions of excitement, especially too violent delirium, are present in the initial stage, then we are obliged to combat them with suitable sedatives, such as potassium bromid, chloral hydrate, sulphonal, and finally even morphin, and we may also have recourse to prolonged, lukewarm, full-length baths as adjuvants to the above-mentioned medicinal measures to quiet these turbulent symptoms. But if, as is rarely the case, a threatening weakness of the heart is noticeable in the initial stage, then it is, of course, advisable to prescribe caffein or camphor (each of them internally or subcutaneously) in the proper doses.

With the transition of the disease into the period of eruption, in all those cases whose further course changes to a typical varioloid, the improvement of the general condition is so rapid and at the same time so permanent that any further general and active medicinal measures are from that time superfluous. Leaving out of view certain local measures which may be desirable in relation to the skin exanthem and the changes in the mucous membranes (see below for particulars), it is therefore allowable, and at the same time quite sufficient, to treat these cases, from the beginning of the eruption, in a purely dietetic manner. And as the digestive apparatus of these patients within a very short time functionates nearly or quite normally, it is not necessary, in the absence of fever and with the appetite regained, to withhold for any length of time a rather substantial dietary. We can soon unhesitatingly give such patients the diet of a convalescent, such as tender, juicy roast beef, vegetables, and the like, besides strong soup and some wine ; and, advancing gradually, their dietary can more and more approach that of health. Only the foods that are difficult of digestion or that disturb the stomach should be, for well-known reasons, avoided for a certain length of time ; likewise sharp spices, as condiments, are to be avoided because of their irritant action on the pathologically affected mucous membranes of the mouth and throat.

For the severe cases of smallpox, variola vera, and variola confluens, very important therapeutic indications present themselves in the further course of the disease, from the local inflammatory symptoms in the skin and mucous membranes during the period of suppuration as well as from the pathologic general condition or the secondary toxemia, which develops more or less strongly during suppuration and which originates from it. But unfortunately it has not yet been given into the power of treatment always, or even approximately always, to exor-

cise to the desired extent the serious dangers which are often present in this stage. It is for this reason that, with the greater violence of the symptoms, the deleterious result of the disease is often, in spite of all our efforts, unavoidable; and, indeed, the same remark might apply to the treatment of the local symptoms connected with the skin and mucous membranes, as to that of the general symptoms which accompany the disease (the fever and the other signs of blood-poisoning).

For the local treatment of the smallpox exanthem on the skin, numerous methods have been proposed and employed in order to lessen, in the face, the violence of the inflammation, and, where possible, to take from it its destructive character. Physicians have for this purpose opened the smallpox pustules separately and evacuated the pus, and afterward cauterized the base of the opened pustule with the silver nitrate point used in opening them. This method, practised by the early Arabian physicians, the so-called ectrotic—from ἐκτιτρώσκειν, "to cause a miscarriage," "to make abortive"—treatment of the smallpox pustule, is applicable only to cases in which the pocks are few and widely separated, hence to relatively mild cases. In the cases in which the pocks stand closely crowded together, on the other hand, or in variola confluens especially, the method is entirely impracticable. But even in the former class of cases, the milder cases of variola vera discreta, it is now generally abandoned, as its advantage is problematic and the whole proceeding is as tedious as it is painful.

Among the means which have been believed to have a specific influence on the smallpox exanthem, and which have, for this reason, been employed preferably locally on the skin, is to be mentioned the quicksilver method. This method was formerly frequently applied to the skin of the face of the smallpox patient at the beginning of suppuration, sometimes in the form of a salve and sometimes in the form of a plaster (Emplastr. mercuriale simplex, Emplastr. mercuriale de Vigo), the face being thus kept covered for several days. The result which was often observed was a very marked abatement in the tense and painful sensation in the skin; apart from this, there was no result, or none worthy of note, as neither a more rapid course of the suppurative process nor a less violent character of it has been reported in the cases so treated. This method has therefore been entirely abandoned now, and it has been recognized that the analgesic peculiarities of the quicksilver application mentioned were due exclusively to the fatty and oily constituents, and may be brought about by the influence of a covering with these latter; this influence may be just as well secured by the application of a piece of pork rind to the skin, by the use of oily compresses,

by vaselin applications, etc.   Another method of applying the quicksil-
ver to the skin, which has found and still has its admirers, consisted
and consists in the use of sublimate poultices (as in erysipelas).   I
myself used this method for some time in variola, but afterward gave it
up, as I failed to see any decided influence on the suppuration process
which I could ascribe to it, and simple poultices of pure water seemed
to furnish me with an equally good application, so far as the analgesic
effect was concerned.   (See below for further details.)   In consideration of
the great toxicity of the sublimate, I deemed it so much the more advis-
able to use simply water for the local application instead of the solution
recommended (1 : 1000, according to Skoda's formula).

Of other measures which have been praised as having great influence
on the smallpox exanthem in the skin, we might further mention the
early and frequent painting of the skin of the face with solutions of
lunar caustic, but especially with dilute tincture of iodin (Tinct. iodi and
Spir. vini rectif., āā partes æquales).   This method, if used once daily
from the time of the eruption, is said to limit the exanthem in its further
development and to cause early desiccation locally (Martius, Eimer,
Knecht).   Further experience has unfortunately shown that, in spite of
these weighty recommendations, the praise bestowed on this method is
not entirely deserved, and that in really severe cases of smallpox the
method exerts by no means the influence which was hoped.   The same
is true also of the internal use of *Sarracenia purpurea* (Fleischmann), of
the internal and local use of xylol (Zuelzer), or of carbolic acid and
other disinfecting agents.

In later times we are, as I believe rightly, turning more and more
from the use of severe measures and supposed specifics against the exan-
them of smallpox, acting upon the view, which is certainly not a preju-
diced one, that among all the methods proposed up to the present time
not one deserves the name of an abortive measure.   The advice of F. von
Hebra is therefore being followed more and more ; he saw the best
results for the patient, so far as regards alleviation of the pain and gen-
eral quieting of the patient, come from the frequently repeated applica-
tion of moist cold (in the form of ice-water compresses or other moist,
cold packs) to the skin which was covered with the smallpox exanthem.
By this relatively very simple procedure we do not, to any greater
degree than by any other methods, effect that in cases of variola which
are at one time severe, the suppuration process shall not penetrate deeply
and shall not afterward leave behind scars in many places ; but these
dreaded marks of the disease do not result any more frequently after
the use of this method than after any other, nor are they in any way

more permanently disfiguring. And because Hebra's method undoubtedly helps the patient, in case he survives, it should, in my opinion, be given the preference over others for clinical use, until something better shall have been discovered. While it is recommended, during the advancing period of suppuration, to cover the portions especially visited by the exanthem (head and face, later hands and feet) with frequently changed ice-cold compresses, it is pleasant to the feelings of the patient when the inflammation has reached its highest point to arrange that the temperature of the water, while still cool, should yet be somewhat higher; to leave the compresses longer in position, and to provide them with a waterproof or protective cover; in other words, to make a so-called Priessnitz poultice. If in the progress of the suppuration the odor of the decomposing pus on the surface of the body becomes more and more unpleasant, then the addition of carbolic acid, or potassium permanganate, or thymol to the water of the poultice may be efficacious.

If we combine the local use of moist cold on the head and face, hands and feet, with the intermittent application of moist cold coverings over the rest of the surface of the body, then the procedure described becomes an antipyretic measure. We cannot, of course, depend on this plan for any very considerable antipyretic effects; such effects are not even produced in the suppurative fever of severe cases of variola by the cold baths, nor to any decided extent by the ordinary doses of antipyretics which are used internally. Whereas, too, an increase of the dose of these antipyretics—phenazone, antifebrin, and the like—is attended by the danger of a collapse, and whereas, on the other hand, cold full-length or reclining baths for variola patients in the suppurative fever must, without exception, be recommended with the greatest caution, the afflicted patients are well pleased to allow their sore and painful bodies to be wound with coverings of wet cloths, and often feel themselves subjectively not a little relieved by these measures.

[So far as the face is concerned, great relief is obtained by the application of a light mask of lint, thoroughly soaked in a mixture of iced water and glycerin (a teaspoonful to an ounce of water) and covered with oiled silk. In the earlier stages of the rash also antiseptic and astringent dusting-powders will possibly relieve the distressing heat and irritation of the skin. Boric acid, "dermatol" (subgallate of bismuth), "Emol keleet" (which is a refined fuller's earth), or a carbolized zinc dusting-powder may be recommended. The formula for the last-named application is as follows: Liquefied pure phenol, half a dram to a dram; oxid of zinc and lycopodium powder, of each, one ounce. McCombie observes that many patients prefer to have no applications

whatever on the skin. At the same time he strongly recommends the early separation of the crusts, whether on the face, scalp, or elsewhere. This, in his opinion, can best be accomplished by the application of linseed-meal poultices, sprinkled with iodoform. On the face the method most agreeable to the patient is to cut a mask of a single thickness of lint, with apertures for the eyes, nose, and mouth. Then to smear a thin layer of linseed-meal poultice on this, taking care to put on the surface a little vaselin in which iodoform has been mixed, and to apply this poultice to the face, changing it every two hours. The treatment of smallpox by the continuous warm or tepid bath has been strongly advocated by Hebra, Stokes and Hawtrey Benson, of Dublin, and others.*]

[The red light treatment of smallpox has in recent years attracted much attention. It will be remembered that John of Gaddesden, in the fourteenth century, surrounded his smallpox patients with red curtains, red walls, and red furniture of all kinds, for in this color there was, he averred, a peculiar virtue. After the lapse of five centuries the therapeutic skill and clinical acumen of the "Rosa Anglica" are vindicated so far as the treatment of smallpox by red light is concerned. In 1871, J. H. Waters, of London, and W. H. Barlow, of Manchester, bore testimony to the usefulness of the exclusion of light in the treatment of smallpox. In a suggestive paper on the effects of light upon the skin, Niels R. Finsen, of Copenhagen, in 1893, suggested the treatment of smallpox by complete exclusion of daylight; or, what would doubtless have the same effect, by the use of tightly closing red curtains, or, better still, windows of red glass. Effect was given to his views with success by Lindholm and Svendsen, of Bergen, in the same year. Since then, Juhel-Renoy, of Paris, J. Marshall Day and J. W. Moore, of Dublin, Feilberg, of Copenhagen, and others, have borne witness to the advantages of this method in checking inflammation of the skin in smallpox and so limiting the amount and intensity of the eruption. The view that it is the chemical and not the caloric rays of the solar spectrum which are active and have to be intercepted, and also that the skin affection induced by strong electric light is identical with solar erythema, was first advanced by Charcot in 1859, but was not proved scientifically until 1889, when Widmark, of Stockholm, determined that it is exclusively the chemical rays in sunlight, especially the ultra-violet rays, which are active in causing both pigmentation and solar eczema. The so-called chemical or actinic rays, which are essentially situated in the blue and violet, and

* *Dublin Jour. Med. Sci.*, vol. LIII, 1872.

especially in the ultra-violet, part of the solar spectrum, are the most refrangible of the rays of light. In this area the chemical activity is strongest, the caloric energy is weakest. The converse holds good in the other end of the spectrum, where are found the red and ultra-red rays, which are the least refrangible. Here the caloric activity is greatest and the chemical activity least.]

[C. Feilberg, senior physician at the Oresund Hospital, Copenhagen, treated fourteen cases of smallpox by exclusion of the chemical rays of daylight in a sporadic outbreak in Copenhagen in January and February, 1894 (Hospitalstidende, July 4, 1894). In an epidemic in Dublin in 1894–1895, the smallpox patients in Cork Street Hospital were subjected to the red light treatment. John M. Day, the resident medical officer, reports that with the use of red blinds eye troubles ceased to appear, the patients rested well and spoke of the color as soothing. Day considers that pitting is less under this treatment, which also obviates the necessity of applying bandages over the eyes and masks to the face. Pigmentation of the skin of the face was lessened. He incidentally mentions that while the red blinds were kept down, the patients were not nearly so much troubled with flies.]

The treatment of the variolous affections of the mouth and throat require, in addition to the local applications of cold, in the form of ice-cravats around the neck and pieces of ice held in the mouth, the use of astringent gargles and mouth-washes. For the latter purpose, dilute solutions of liquor ferri perchloridi or of chlorate of potassium are especially appropriate. For children who do not know how to gargle, it is necessary to wash out the mouth and throat carefully with such a solution several times during the day. Besides this, it is recommended, where there is greater pain and where sore spots are present in the mouth and throat of the patient, that washes and gargles be made with the mucilaginous and bland decoctions of marshmallow or althæa, and that thin oatmeal gruel or barley gruel be constantly given to drink. Larger ulcers must be touched with silver nitrate or painted with liquor ferri perchloridi. Abscesses of the tonsils or of the tongue should be opened early, and if edema of the glottis occurs, attempts should be made to scarify it, or it would be better to resort at once to tracheotomy.

With regard to the further treatment of severe cases of smallpox during the suppurative period, it should be remarked first that the greatest attention should be paid to the feeding of the patient. It is, of course, impossible at this time, when the high fever has returned, when the anorexia is complete and deglutition is extremely painful to the patient, to give very substantial nourishment; but, on the other hand, one

must not neglect, with the view of preserving the patient's strength, to give milk regularly at not too long intervals, meat broth with the yolk of an egg stirred in, gruel (see above), etc. In addition to this, the patient, who is usually tortured by thirst, needs frequently small amounts of cooling drink (water, best pure or with the addition of a small amount of lemon juice or raspberry syrup, in the form of lemonade). In the stage of the disease of which we are speaking, the most pressing question is what is to be done to combat the general toxemia, and whether it is possible to influence this in any way favorably by means of therapeutic measures. Although it must be repeated that really active means to combat this dangerous general condition do not, unfortunately, stand at the behest of treatment, yet it appears to me that we are not, on the other hand, quite helpless. I would suggest that a combination of means which are effective in other infectious conditions which have a purulent basis should not be left untried in the suppurative fever of variola. I mean the use of large daily doses of alcohol in suitable form, and the simultaneous use of strong decoctions of cinchona bark. In my clinic I have for years made regular and combined use of these two remedies in suppurative fever of severe cases of variola, and I believe, on the basis of an unprejudiced estimate of the results, that I can truthfully assert that there is indeed a certain positive therapeutic value in the suggested combination. In variola purulenta febrilis I use the alcohol exclusively in the form of cognac (best quality), for adults not less than 60.0 (about 2 fluidounces) per diem, according to the individual tolerance, but often considerably more (100.0 to 120.0 per diem). I never let him take it raw on account of the irritating effect on the mucous membranes of the mouth and throat, but always have it diluted. For purposes of dilution, pure water serves in part; while for the other part, I use yolk of an egg as an emollient and at the same time a nutrient. As a suitable form for the administration of the cognac, among others the well-known Stokes's formula recommends itself; it has been used in many places in febrile conditions of other kinds, and is to be especially recommended in variola. As concerns the decoction of cinchona bark, I might remark in passing that I am so old-fashioned as to decidedly prefer it to quinin (and also to the other single cinchona alkaloids in pure form) in combating the purulent infectious diseases. I have come back to it again after I had, for a long time in those same forms of disease, used those alkaloids themselves, but with not as good results. I usually prescribe the decoction of cinchona bark for the variola patient in the suppurative stage with an addition of dilute hydrochloric acid, and a further addition of

spiritus ætheris nitrosi, which latter preparation, in the adynamic states of the disease, is known to add to the good reputation of the remedy.

Something further is necessary to complete this summary of the treatment of the stage of suppuration, and I would not pass over it in silence ; where high febrile temperature exists, and with it a restless cerebral state of excitement, which threatens to exhaust the patient, then modern pharmacology possesses in lactophenin an excellent remedy, which, besides lowering the temperature without injury to the patient, possesses also peculiarly sedative properties (A. Jaquet). In the last epidemic at Basle (1894), in which I was called upon to treat in the clinic at the isolation station, not only a large number of mild cases, but also some very severe cases of variola (discreta and confluens), we tried in the latter, during the suppurative stage, the new medicine (given in doses of 0.5 once or twice toward evening), which had repeatedly before given good results in typhoid fever, pneumonia, etc., with severe cerebral symptoms. I cannot now help, after the experiences of the last year (1895), adding these few words concerning the use of lactophenin in variola suppurativa under the above-named conditions, as the influence on the fever and also on the general condition was extremely favorable. Of the other means of combating the delirious condition we may, naturally, name chloral hydrate (best administered in the form of enema), potassium bromid (likewise in the form of enema), opium, and, finally, protracted lukewarm baths, which also relieve the patient's subjective symptoms.

A careful control of the heart-rate and pulse is of the very greatest importance. As soon as any disturbing symptoms of excessive frequency, weakness, and irregularity begin to make their appearance, then we must without delay counteract them by means of the most powerful restoratives, as camphor and caffein. These two remedies are best exhibited alternately, in not too small and in frequently repeated doses given subcutaneously, as in this way a restorative influence is most quickly and most surely rendered available and the stomach of the patient suffers no irritation. This stimulating method forms also the real foundation of the treatment in those otherwise hopeless cases of purpura variolosa, and even if the patients cannot be saved, yet they avail, it may be, to delay somewhat the fatal termination.

Some complications of the disease which occur during the period of suppuration, and are very purulent in their nature, must be considered and treated according to the rules laid down for their management. Accessible abscesses, especially, are to be opened early, and pleural

effusions, if purulent, are to be evacuated ; the same is true of vario-
lous inflammatory conditions in the joints, etc.

In the cases of pustular variola tending to improvement, when,
after safely passing the critical point of the disease, abatement of the
fever, desiccation of the exanthem, and other encouraging symptoms
become noticeable, we may, as a rule, leave the therapeutic measures
hitherto used in the background, and concentrate our attention on a
simple nourishing treatment of the patient and convalescent.   The time
when this simplification of the treatment may take effect is regulated in
each individual case by the circumstances.   In relation to the feeding
of the convalescent, variola furnishes no exception to the rules laid
down for treatment after other severe and exhausting acute diseases ; on
the other hand, the care of the skin deserves especial attention.   It
may be remarked, first, that by protracted lukewarm baths to which a
little bran has been added the unpleasant itching and irritation of the
skin during the period of desiccation are somewhat relieved.   Later
on, soap and water baths, repeated daily, may properly take the place
of those above mentioned, in order to hasten the separation of the scabs.
One should, however, never attempt in the bath or outside of it to re-
move by force the scabs which cling somewhat closely, but those which
are ripe for shedding—that is, those that are easily removable—may be
loosened at times with great care.   If during decrustation especially
large and firmly adherent scabs have formed anywhere, as in places
where local confluence of the pocks has been present, and we have
grounds for supposing that there is under them considerable loss of sub-
stance, then, naturally, the prudent measures just mentioned should be
especially attended to.   Until, in such places, the loosening of the scabs
takes place spontaneously, we may cover them with a vaselin bandage
in order to protect them from the scratching hands of the patient and
at the same time to relieve somewhat the unpleasant tense and itch-
ing sensations which are present.   When, after loosening of a scab, a
sore, unhealed spot appears, proper bandages, moistened with lead-lotion,
boro-vaselin, or the like, should be applied locally for a time until the
place heals properly.   Excessive granulations are to be treated, as else-
where, with a pencil of silver nitrate, used once or repeatedly as may
be necessary.

Among the sequelæ of variola which occur on the skin may here be
mentioned, with especial reference to its treatment, the furunculosis
which so often appears and is so obstinate (compare the earlier state-
ments).   In addition to the necessary surgical treatment (opening of the
ripe furuncles), this condition requires internally the renewed use of

the decoction of cinchona bark and an especially nourishing, predominantly animal diet. The same is true for the acute bedsore which is sometimes somewhat persistent.

Disfigurements of the face by smallpox scars may be guarded against in advance in severe cases of variola (see earlier), or they may be somewhat improved after they have actually occurred. Wherever the cutis is directly attacked by the suppurating process in the papillæ, the subsequent filling of the defect by the formation of scar tissue forms the only natural method of cure, which cannot be much altered. We can, according to Buri's proposal, attempt, by repeated application of resorcin paste to the affected parts, to compel the newly formed skin to exfoliate repeatedly, the remains of the papillæ to become gradually elevated, and, finally, under zinc paste bandages, to allow the healing to become complete. I have myself had no experience, however, and can say nothing as to the real benefits arising from this cosmetic procedure, by which the scars are said to become less deep. The safest way of avoiding smallpox scars is, in general, to destroy the susceptibility to the disease, or so far to weaken it that, if the disease is actually acquired, it shall assume only the mild form. All this is assured, however, according to our present ability and knowledge, only by the careful and most general use of vaccination and revaccination, which is, at the same time, the only proved means of combating the miseries and dangers of smallpox.
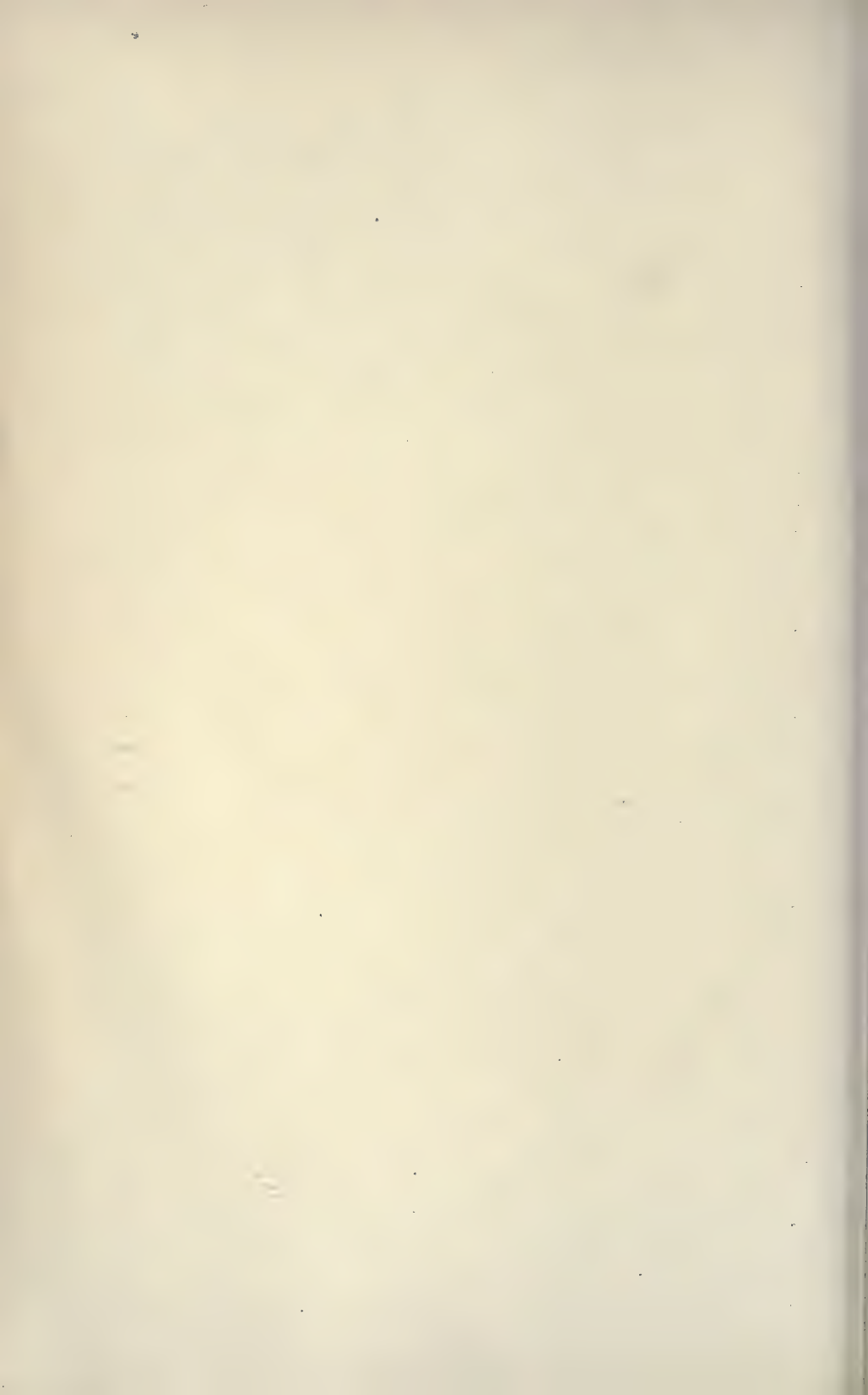
VACCINATION.
(INCLUDING VARIOLATION.)

BY

H. IMMERMANN, M.D.

VACCINATION.

(INCLUDING VARIOLATION.)

GENERAL CONSIDERATIONS. DEFINITION.

SINCE the time of Jenner (1798), we understand by vaccination a prophylactic measure directed against variola, having for its object the production of immunity to this disease, and consisting of inoculation with the contents of the vesicles of vaccinia, or cow-pox. Vaccinia, or cow-pox (*vacca*, " a heifer "), was originally a peculiar localized exanthem resembling that of smallpox, which sometimes appeared on the udders of milch-cows. The individual vesiculopustular pocks composing the exanthem were designated as original or natural vaccinia, and also as cow-pocks in the more restricted sense. In addition to this, all pocks produced directly or indirectly by an original vaccinia were also called vaccinia, or cow-pox.

It has been known for a long time that the original cow-pox is contagious, and that it is capable of inoculation by means of a virus contained in the pocks. With the exception of rare and doubtful instances, this inoculated cow-pox always remains local, neither occurring at points removed from the site of inoculation nor becoming generalized, and pursues a course similar to that of the original vaccinia. The inoculation may be either accidental or intentional. The intentionally inoculated vaccinia is designated as artificial vaccinia, in contradistinction to cow-pox occurring naturally or acquired by accidental means.

Vaccinia may be transmitted to other individuals of the bovine species, and this vaccinia, which is regularly cultivated within the species and which resembles the original in all respects, is usually known as animal (more correctly, bovine) vaccinia. A vaccination performed with such animal (bovine) virus is usually known in medical parlance as an animal vaccination.

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The susceptibility to the *virus vaccinale* is, however, not limited to the bovine species, but extends to a great many others, the most important of which is the human species. Vaccinia transferred to man (or humanized) remains unchanged in all of its essential peculiarities, and may be inoculated from individual to individual without developing any marked variations. Finally this human vaccinia may be readily inoculated back again into cattle, and the local eruption of this "retrovaccinia" resembles the original or natural cow-pox in all respects and is equally capable of transmitting the disease. From all that has been said, it is clear that vaccinia is the same disease in the human and bovine species at least.

The same agreement exists in reference to the prophylactic effect of all these differently produced forms of vaccinia. The prophylactic value of every correctly performed and successful vaccination —whether the virus be bovine, human, or retrovaccine—always manifests itself in man and cattle by the production of an immunity to vaccinia and to variola. This immunity is probably a permanent one for cattle; in man it lasts for a number of years at least. It is this fact that makes vaccination so important a precautionary measure in the prevention of one of the most devastating diseases (variola), and that also makes it so significant a factor for the general good. Among the Germans vaccinia is consequently known as the "protective pox."

By revaccination, which must not be confounded with retrovaccination, we understand the renewal of the vaccination (with bovine, human, or retrovaccine virus) for the purpose of renewing the protective period in previously vaccinated individuals. Experience has shown that the period of protection against both vaccinia and variola after a single successful vaccination is not a permanent one in man, and that the susceptibility to these diseases frequently returns by degrees. This unfortunate recurrence of susceptibility may be prevented by a successful revaccination, which will temporarily restore the protection against both vaccinia and variola. It is possible, by repeated revaccinations at regular intervals, to maintain this protective period any required length of time. Revaccination is consequently of great sanitary importance as a supplementary measure to the primary vaccination, and is also of value since it demonstrates by its results the extent to which the susceptibility has recurred in the previously vaccinated individual.

By variolation we mean the inoculation of smallpox, or variola. The effect of this procedure, which was carried out as a prophylactic

measure before the introduction of vaccination, is the production of a local variolous eruption at the point of inoculation, to which is usually added a true attack of smallpox with a high fever and a generalized exanthem. The inoculated individual commonly acquires a permanent immunity to variolous affections for the remainder of his life, as is also the case when an individual has an ordinary attack of smallpox.

If human variola is inoculated into cattle, there is no general eruption, but simply a local one at the point of inoculation. The result is practically the same as that obtained by the inoculation of cattle with vaccinia. At the present time we designate such a pox in cattle, produced by inoculation with variola, as variolo-vaccinia. This disease may be continuously inoculated from one member of the bovine species to another, losing neither its local type nor any peculiarity of its virus; and, what is more remarkable, if inoculated back into man, it still acts simply as vaccinia. In addition to cattle, some other animal species are also susceptible to variolation. In the majority of instances the result is similar to that obtained in cattle, but certain variations are observed dependent upon the species.

The preceding general definitions and deductions serve merely as an introduction to the subject in detail. More definite information concerning the important subject of the prophylaxis of variola in the individual will be found in the succeeding sections. Since the inoculation of human smallpox or variolation is by far the oldest method of immunization, it should naturally receive our attention first.

LITERATURE.

The literature of vaccination is scarcely less voluminous than that of variola. In the following bibliography only the more important works and treatises upon the subject can in consequence be mentioned. Since the majority of writers since the time of Jenner have treated of variola and vaccinia together, the general literature of vaccinia will be found in no small part included in the literature of variola. In a number of special sections in the following consideration of the subject, separate literary references in special bibliographies will be required. These will always be found at the close of the particular section, as is also the case in the section upon "Variola."

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THE INOCULATION OF HUMAN SMALLPOX (VARIOLATION).

HISTORY.

Accounts of the inoculation of human smallpox may be found in the records of the most ancient times. Long before the beginning of our chronology, variola was purposely inoculated as a prophylactic measure in Hindostan and in China. These historic data concerning the inoculation of variola also furnish a very important evidence of the great age of variola itself in these two countries. (See the historical sketch under "Variola," p. 14.) The constantly repeated observation that the individual is commonly attacked by smallpox but once in a lifetime apparently gave rise to the origin of the custom. All further efforts were directed to those preparatory measures and methods of symptomatic treatment which made the inoculated smallpox as benign as possible.

The methods of transmission were entirely different in India and in China. In the latter country the procedure never progressed beyond a rude and primitive form; they contented themselves with either simply clothing the individual to be inoculated in a shirt impregnated with variolous pus or stuffing dried smallpox crusts into their noses! We are unable to draw any very definite conclusions concerning the results of these repulsive procedures. They frequently failed, and they still more frequently led to the most severe attacks of variola. To the best of our knowledge, it is nevertheless true that in China the method never progressed beyond this stage (Kirkpatrick). In Hindustan, on the contrary, the method of inoculation commonly performed, even at a very early date, was much more elaborate and, at the same time, more sensible (Holwell). It was intrusted entirely to the priests, who traversed the country every year at the close of the cool season and before the period of great heat, and who required those individuals desiring inoculation to undergo a preparatory dietetic treatment (abstinence from milk and fish) of four weeks' duration. The inoculation was always performed in the open air. The virus was introduced by means of scarifications made upon the outer surface of the arm or forearm. The incisions were 15 or 16 in number, parallel, and about ½ inch in length. The entire extent of the scarified area was immediately covered with a compress of cotton-wool which had been impregnated with the virus and moistened with the water of the Ganges. They never employed a fresh virus, or that of an accidentally acquired case of variola, but always used a virus obtained from an inoculation of the preceding year. From the time of the inoculation until the disappearance of the smallpox, the inoculated individual was compelled to remain in the open air and was rigidly ex-

cluded from intercourse with any one but the priests. They ate bland foods, drank cold water abundantly, and were at first treated with cold irrigations twice daily. The contents of the inoculated pocks were carefully pressed out before the appearance of the general exanthem. The results of these old Indian methods of inoculation, which with some slight modifications were still carried out until more modern times, seem to have been very good. Fatal cases, at least, were almost unknown.

In addition to Hindustan and China, with their primitive methods of procedure, other portions of the eastern hemisphere were acquainted with and practised inoculation at an earlier date than Europeans. It has been established that prophylactic inoculation was practised by the inhabitants of Barbary and Senegal in Africa, and by the Circassians and Georgians in Asia, before it crossed the Bosphorus from Thessaly to the Fanariots, of the Greek colony in Constantinople.

It soon happened that the procedure was brought to the notice of Lady Mary Wortley Montague, the wife of the English ambassador at Constantinople, and she had so much confidence in it that she allowed her six-year-old son to be inoculated by a Greek physician in 1717. When she returned to England four years later (1721), she allowed Dr. Maitland to carry out the same procedure upon her daughter, who had meanwhile attained the age of six years. In both cases the course of the inoculated variola was mild and favorable, and the occurrence naturally caused considerable comment, not only in England, but also elsewhere. This was the beginning of that memorable spreading of the procedure throughout the countries of Europe during the eighteenth century (or until the appearance of Jenner).

In England, the example of the courageous woman soon found ardent followers, and in the immediately ensuing years a considerable number of inoculations were made, especially at court among the gentry. The results fulfilled all expectations, inasmuch as bad terminations were rare in these early cases of variolation. They were not completely wanting, however, and it is quite certain that it would have been more fitting to have paid greater attention to the selection of the virus than to the other details of the procedure. Instead of this being done, however, the enthusiasm soon deteriorated into a craze, which was largely administered to by charlatans and quacks, the regular profession rather holding themselves aloof from the general public. The bad consequences of these foolish and widespread procedures were not long in making their appearance, and ten years after the introduction of the method of inoculation, the mortality of inoculated variola had increased at a most alarming

rate. The physicians, and especially the clergy, now raised the voice of warning against inoculation, with such good effect that a reaction soon occurred. Fear took the place of confidence, and the advance of inoculation was so impeded that toward the middle of the eighteenth century the procedure was almost brought to a standstill.

On the Continent, inoculation also excited general interest at first. It was not generally tested, however. Only a few physicians made any extended use of the innovation, and they did it most hesitatingly. The majority of the medical profession and the general public looked upon the procedure with distrust. This distrust was still further increased by authoritative influences, among which that of de Haen became of historic importance in the later development of variolation. De Haen, from the beginning a most violent opponent of inoculation, never tired in his opposition to the procedure, and thanks to his high scientific position, he naturally found the greatest number of followers for himself and his opinions. On the other hand, it was his lack of moderation, in attacking the entire principle of the method and his complete misconception of its good points, that caused others to fight righteously for the procedure. It is certainly remarkable that the same man who may be safely designated as the fiercest enemy of inoculation, and who used his best efforts to defeat it, was also largely responsible for the introduction of the procedure into renewed favor.

In due time he found some opponents who were equal to him in mental capacity and who unquestionably surpassed him in prudent judgment. These individuals attempted to determine the true value of inoculation from statistics made up from their own experience and that of others, and they independently reached a conclusion that was favorable to the procedure. They were able to show, by the help of the numeric method, that without being prejudiced by many dangerous terminations in individual cases, inoculation on the whole was better than blindly trusting to the fate of acquiring the disease naturally, that it had a lower rate of mortality, and that the method itself deserved conditional recommendation. At about the middle of the eighteenth century, it consequently happened that de la Condamine in France, Tissot in Switzerland, Hensler in Germany, and many others caused a reversal of the existing popular opinion by their arguments. It was at this time also that inoculation found a most independent and brilliant champion in Angelo Gatti (Professor of Medicine at Pisa, later at Paris). With the advent of this man

(1760), who possessed one of the most enlightened minds of all times, a new epoch of inoculation commenced in Europe. This second period of inoculation was of longer duration than the first wild craze; the procedure reached its highest development and did not make its historic exit until the discovery of the procedure of vaccination by Jenner in 1798.

Gatti's services to inoculation principally consisted in an improvement of the method, and especially in a rigid and accurate separation of the superfluous from the necessary portions of the procedure. From conclusions based upon personal experience and upon many observations which he had previously collected in the East (especially in Greece and in Constantinople), Gatti rid the procedure of all those enervating preparatory methods that were then in vogue, being convinced that the unimpaired health of the individual afforded the best and surest guarantee for the success of the inoculation. He exercised the greatest possible care in the selection of his virus, sometimes employing only a very small quantity of lymph from the mildest cases of smallpox. He obtained this lymph when it was still perfectly clear and before it became clouded by pus. Later, he employed only the lymph obtained from the contents of inoculated pocks, never using that from an ordinary case of variola. By the latter method he succeeded in producing a very light attack, as a rule, and he consequently restored variolation to considerable credit and reputation in the second half of the eighteenth century.

In addition to Gatti, there were other men who had special good fortune in the practice of inoculation, and who consequently gained a considerable reputation as particularly expert inoculators. Special mention might be made of Th. Dimsdale and the brothers Sutton in England, of Rosenstein in Sweden, and of P. Camper in Holland. They all practically followed the method of Gatti, although several of them deferred to the prejudice of the people by returning to some of the discarded preparatory procedures.

Although the annual number of individuals inoculated in many European countries (especially in England, but also in Sweden and in Holland) during the last decade of the eighteenth century was rather large, inoculation was never generally employed or even officially sanctioned at any time in its history. There were always two weighty objections to the procedure. The first was the undeniable fact that, in spite of the greatest care in the selection of the virus and despite all other precautionary measures, the inoculated variola sometimes pursued a more severe course than might have been

expected. The second objection was that fatal cases still occasionally occurred. Basing his estimate upon the best obtainable sources, Gregory places the mortality of inoculation in the second half of the eighteenth century at about 1 : 300—a ratio which made one pause for consideration before submitting to such a prophylactic measure. It must also be remembered that many inoculated individuals recovered with serious impairment of health, because the disease frequently progressed with any number of undesirable complications.

A still more weighty objection than the remote possibility of a severe termination, was the fact that inoculated smallpox acted exactly like natural smallpox, in that it was transmitted by means of a volatile contagium, and that inoculation favored the spread of the disease and even the development of epidemics. If proper precautions were not observed, the inoculated individuals not rarely transmitted variola to their immediate and remote surroundings by means of the volatile contagium in their exhalations, and these secondary cases of variola were by no means as mild as the original cases of variolation. In its earnest endeavor to lessen the dangers of smallpox, inoculation without doubt had something, and probably a great deal, to do with the further spread of the disease. This was certainly an unanswerable reproach to the procedure.

Consequently, when Jenner (1798) made known his protective method of vaccination, pointing out the benign character of cow-pox for the vaccinated individual, and emphasizing the fact that vaccinia was not transmitted by a volatile contagium, he indirectly pointed out in the most marked manner the two great and ineradicable defects that cling to inoculation. It was not astonishing that Jenner's method rapidly superseded inoculation, especially after the correctness of his statements had been very generally verified. In civilized Europe, at least, the fate of inoculation was sealed, and the procedure soon passed out of use. Inoculation succumbed, but her fall was no inglorious one, for she fell before the power of a superior opponent. For all time to come, it may be said of inoculation with a better right than of many another transitory procedure in the realm of medical prophylaxis, "*In magnis voluisse, sat est!*"

It is worthy of note that isolated inoculations were performed in England, the cradle of vaccination and the home of Jenner, until 1840, when they were prohibited by law. In Continental Europe the practice had already been either long abandoned or forbidden. In many places outside of civilized Europe (in Hindostan, in China, and among the native population of Algeria) inoculation still exists at the present time as a customary and valued prophylactic measure against variola. There is

also very little likelihood that vaccination will ever supplant inoculation in those countries, since the native population cherish too strong a hatred against any variety of European influence, and because this hatred will be continually nurtured as a part of their religion.

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INOCULATION VARIOLA IN MAN.

The inoculation of variola in man does not claim that prominent position in modern clinical medicine which it naturally did in the medical world of the past. Its clinical appearance is nevertheless worthy of our attention, not only from the standpoint of historic interest, but just as much so from our desire to thoroughly study the smallpox problem by viewing it from all sides. The clinical picture of inoculated variola that has been handed down to us in the writings of the foremost inoculators of the eighteenth century has features which differentiate it from the picture of ordinary variola, and these features were also sharply emphasized by the authors themselves. From a symptomatic point of view, the inoculated variola of the last century holds a peculiar middle position between modern variola and modern *Vaccina humana,* and seems to form a connecting-link between the two. It is consequently clear that a brief consideration of the clinical course of inoculated variola is of considerable importance for

the understanding of the relations existing between the two diseases (variola and vaccinia).

Some facts about the subject under discussion will consequently be given as they are found in the authoritative descriptions of special writers upon variolation (Gatti, Tissot, Dimsdale, Camper, Rosenstein, Hufeland, and others). These observations will be briefly prefaced by a few data concerning the hygiene and technique of inoculation in Europe (from the same sources).

Childhood was regarded as the most appropriate age for the performance of inoculation, and indeed many inoculators preferred to carry out the procedure upon sucklings in the first six months of life (Locher). Others preferred to wait until the end of the first dentition, and inoculated between the third and sixth year. Inoculation was still regarded as a relatively insignificant procedure for the inoculated individual until the end of the twentieth year, while frightful pictures were painted of its dangers in elderly persons, and especially in pregnant and puerperal women.

The individuals to be inoculated were usually previously isolated for a certain time (ten to fourteen days). This was for the purpose of protecting them from an accidental infection with smallpox during this preparatory period. The actual preparation consisted of a moderate restriction of the diet, and usually also of the administration of mild laxatives.

The inoculation itself was performed by some with the inoculating needle or lancet (Dimsdale); others applied small blisters and then caused the raw surfaces to be impregnated with the virus (Hufeland). The material used for inoculation in later times was almost without exception the clear lymph (not clouded by pus) from the well-developed pocks of an individual who had been inoculated a short time previously. The usual site of application was upon the upper arm, the lymph being deposited upon two or three areas upon both upper extremities.

The course of the inoculated variola could be divided into certain periods, which followed each other in regular order and were usually as follows:

In the first period (latent or incubation period), which comprised about three days, no local reaction could be observed at the point of inoculation, and the general condition of the inoculated individual was completely undisturbed. Commencing with the fourth day, signs of local reaction were noticed at the site of inoculation; there arose papular elevations, which gradually became transformed into

typical loculated variola vesicles with clear contents (period of local reaction). The greatest development of these local smallpox vesicles was usually reached by the seventh day or even somewhat sooner; the entire field of the inoculation became red, swollen, and inflamed, and the contents of the pock became clouded with pus. At the same time the inoculated individual had an active fever and other symptoms of a disturbed general condition. This stage (local maturation and general febrile reaction) usually comprised another three days (lasting from the eighth to the tenth day from the date of inoculation), and was then usually followed by a rapid fall of temperature and an improvement of the general condition. With the fall of temperature (usually upon the eleventh day) a generalized variolous exanthem almost always appeared upon the body of the inoculated individual, while at the same time the original pocks exhibited distinct signs of beginning desiccation. After the appearance of the secondary variolous exanthem upon the remaining portions of the body of the inoculated individual, the inoculated variola acted just like an ordinary case of smallpox, and was capable of following a variable course.

As a rule, however, the further course of the disease was not of particular severity if all the approved precautions had been carefully observed before and during the inoculation. There was a considerable variation in the number of secondary pocks in individual cases, but they were never excessively numerous. The pocks usually numbered between 50 and 400, rarely more. Finally, the secondary exanthem was entirely wanting in some cases (variola sine exanthemate) or was only sparingly present and confined entirely to the skin. The secondary pocks passed through the usual papular, vesicular, and pustular stages; intense local suppuration was, however, uncommon, and a marked degree of suppurative fever was still more rare. The clinical aspect of the disease was more that of so-called varioloid (in the modern sense of the word) than that of true smallpox. Scars nearly always remained at the site of the inoculation after the casting-off of the scabs, but the secondary variolous exanthem was usually of a mild character and healed without the formation of cicatricial tissue. In the majority of cases the convalescence was uneventful. Exceptional cases occurred which progressed with grave suppurative fever, sometimes even terminating fatally, but these were fortunately rare.

The course of inoculated variola which we have just pictured may be compared with two diseases: first, with naturally acquired smallpox,

and, secondly, with vaccinia, as it is seen in man. In comparing the disease to ordinary variola, we are struck by the short duration of the period of incubation. In inoculated variola there are exactly three days before the beginning of the local eruption, and about eight days before the general febrile reaction, whereas in ordinary variola the entire duration of the period of incubation is usually about twelve days. The stage of general febrile reaction, lasting usually three days, and the fall of temperature with the simultaneous appearance of a more or less extensive variolous exanthem over the remainder of the body, do not specially differentiate inoculated variola from a mild attack of the naturally acquired disease. The striking difference between the two is to be observed chiefly in the period of evolution of the disease.

A comparison of inoculated variola with normal vaccinia in man, on the contrary, shows that the periods of incubation and the periods necessary for the development of the local pocks are practically of the same duration. This uniformity is maintained until the height of the pustular stage, but from this point on there is a pronounced difference, inasmuch as inoculated variola is characterized by a marked fever lasting two or three days and followed by a general eruption, while in modern vaccinia the fever accompanying the suppurative stage of the local eruption is usually mild and a general eruption does not occur. In those exceptional cases of inoculated variola in which no general eruption whatever was observed (variola inoculata sine exanthemate), there was a still greater resemblance to modern vaccinia, and the only real difference between the two was in the more intense febrile disturbance in the former.

This parallel between the periods of incubation and evolution of inoculated variola and inoculated vaccinia, which has just been pointed out, is a clinical fact of great theoretic importance. It will be subsequently referred to at an appropriate place, because it is of fundamental significance for the determination of the nature of cowpox in man.

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THE VARIOLATION OF ANIMALS.

Although vaccination very properly caused the rapid abandonment of inoculation as a prophylactic measure in man, variolation gradually became a coveted variety of animal experimentation in the

course of the nineteenth century. Extended experiments of this character have been carried out, and the findings in cattle particularly are worthy of the greatest attention. These experiments were performed for the purpose of more definitely establishing the nosologic relations existing between variola and vaccinia, and to obtain a clearer idea of the character of the latter affection. The second definite purpose of this experimentation was to produce an attenuation of the virus of human variola, if possible, by inoculation from one animal to another, and to render this weakened virus suitable for reinoculation into man. The following statement of the facts will show to what extent these two objects were attained.

Gassner (city physician at Günzburg in Bavaria) was apparently the first to make appropriate experiments upon cattle. In 1807 he inoculated a number of cows with variolous lymph from children who were suffering from smallpox. He observed that 11 of these cows developed local eruptions at the point of inoculation, which completely resembled the pustules of vaccinia, and which were not followed by a generalized eruption. Four children were then inoculated with the lymph from this variolo-vaccinia, and they developed beautiful local pustules but no general exanthem. Independently of Gassner, and at a later date, Brown in England and Macphail (Baltimore) in the United States, are said to have obtained the same result.

Thiel in Kasan (1836) and Ceely in Ailesbury (1838), independently of each other, carried out the investigation upon a large scale. In the beginning, Thiele experimented with dried human variolous lymph, which he greatly diluted with warm cow-milk. Upon inoculating man with this fresh mixture of cow-milk and variolous lymph he obtained marked local pocks, which were accompanied by an intense suppurative fever, but the expected general variolous exanthem did not make its appearance. Pursuing his experiments further, Thiele employed living cattle as the intermediate host for the human variolous lymph, inoculating the virus into the udders and vulvæ of cows, and then subsequently inoculating the disease back again into children. This variolo-vaccinia in the cows always remained local, and the same peculiarity was noted in all the children who had been inoculated from them. The disease could be further inoculated from one individual to another like an ordinary human vaccinia without any recurrence to the type of an ordinary variola, and it was only in the first generations that the accompanying inflammation and febrile symptoms were at all marked. Altogether,

Thiele successfully inoculated more than 3000 individuals in this manner directly or indirectly from variolo-vaccinia, and carried the modified virus unchanged through 75 generations. Ceely proceeded in a similar manner and obtained the same result. He repeatedly and successfully inoculated cows with human variola, always obtaining nothing but local pustules (variolo-vaccinia), and then utilized this animalized virus as the initial virus for successive inoculations in man. In this manner he inoculated more than 2000 individuals, not one of whom had a regular form of inoculated variola, although in some cases the variolous lymph had passed through human individuals about sixty times in unbroken succession. Independently of each other, Thiele and Ceely both proved that this attenuated virus of variolo-vaccinia conferred the same protection against human smallpox as did ordinary vaccinia. They subsequently reinoculated their cases with variolous lymphs of full strength, and although in some instances years had elapsed, these reinoculations were always unsuccessful.

These memorable results of Thiele and Ceely allowed certain conclusions to be drawn in regard to the probable nature of vaccinia. If a something is regularly produced by the variolation of cattle which completely resembles vaccinia in appearance and effect, as was shown in a most comprehensive manner by both these investigators, the thought is at once awakened that ordinary cow-pox is nothing but an attenuated descendant of human variola. This view, which has finally forced itself to the front, would undoubtedly have been the accepted one long ago if other skilled investigators (Sacco, Fröhlich, Bartels) had not regularly failed at first in their repeated attempts at variolation in animals. Reiter had a further and still more contradictory experience. In all of his experiments he was only successful in producing one solitary case of variolo-vaccinia, and the child inoculated with this virus developed a mild general exanthem in addition to the local pustulation. Finally, the misconception of the actual condition of affairs was particularly strengthened by the contrary findings of the Commission at Lyons (1865), consisting of such authorities as Chauveau, Viennois, and Meynet.

Chauveau and his associates subjected a large number of cows to direct variolation, and always obtained nothing but rudimentary or papular pocks; further successive inoculation produced a "still more indistinct" result. On the other hand, when they inoculated a child of three months from this stunted variolo-vaccinia, the infant developed a severe attack of variola. This was naturally a warning for all time

that great caution is necessary in the direct and immediate employ-
ment of variolo-vaccine for the inoculation of human individuals.
This result, together with the outcome of other experiments, caused
the Commission to make an absolute declaration that variola and
vaccinia were entirely different diseases throughout, and that the
one species was never transformed into the other. Chauveau has
rigidly held to the latter view until the present time, and still has a
train of followers in France (Layet and others), and also in England
(Crookshank and others). On the other hand, it must be recognized,
and in my opinion can scarcely be disputed, that the newer and later
experiments in this interesting domain of experimental pathology
are to be interpreted as most decidedly in favor of the opposite
opinion.

Among those investigators who have taken up this problem again
from an experimental standpoint (since 1870), particular mention is
to be made of Senfft of Bierstadt, L. Voigt of Hamburg, Haccius and
Eternod of Lancy, Geneva, Fischer of Karlsruhe, Hime of Bradford,
and L. Pfeiffer of Weimar. The results of these investigations will
now be briefly stated. Variola may, as a rule, be easily transmitted
to cattle if the human virus is applied to extensive surfaces of contact
obtained by scarification or by scraping away the epidermis instead
of being introduced through a simple puncture, and the disease so
produced in cattle always resembles vaccinia. If the precaution is
also observed of inoculating the resulting variolo-vaccinia at least
three times more in succession from cow to cow before the virus is
employed for the inoculation of man, the dreaded return to variola
(Layet and others) may be disregarded, since the variolous virus
seems to have been permanently transformed by cultivation into the
milder virus of vaccinia. Since hundreds of thousands of individuals
have been successfully inoculated with the virus of such transformed
variolo-vaccinia in Germany alone during the last decade, and
since this virus has never produced a single case of variola, it may
be concluded that a most intimate genealogic connection, if not an
absolute identity, exists between variola and vaccinia. (Further
information upon this point may be found in the following section,
upon the Pock Diseases of Animals.)

Similarly to cattle, other species, especially monkeys, horses,
sheep, and goats, are susceptible to variolation, although the results
obtained are not completely identical throughout. There are some
individual differences which are worthy of note, and the statements
of various authors also diverge in reference to certain points. Mention

has already been made (in the section upon "Variola," under Etiology, General Etiologic Facts) of the apparently successful attempt of Zuelzer to produce a true variola in monkeys by means of inoculation with variolous blood and pock-crusts. Monkeys are also supposed to be susceptible to the volatile contagium of variola, since great numbers of them are said to succumb to the disease in the tropics at times when human variola is epidemic (M. Schmidt). In the attempts of Buist, and especially in those of Copeman, to produce variolation in monkeys, nothing was observed except local pustules at the site of inoculation, so that differences of result and observation apparently exist upon this point, the cause of which will require explanation in the future. Horses, like cattle, are insusceptible to the volatile contagium of variola; if they are inoculated with variolous lymph, nothing occurs but a local eruption (variolæ equinæ). If, however, the variolous lymph is introduced directly into the circulation, contrary to the result of a similar condition of affairs in cattle, a generalized variolous exanthem is said to arise (Warlomont). Sheep and goats are generally tolerably refractory to the fixed contagium of human variola, and the reaction to variolation, if it occur at all, will consequently be only a local one in the most successful cases. The position of these animals in regard to animal vaccinia and retro-vaccinia seems to be a somewhat different one. The sheep, furthermore, is subject to a special and peculiar pock disease, differing from variola and known as variolæ ovinæ. (More extended data concerning these points will be found in the next section, upon the Pock Diseases of Animals.)

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THE POCK DISEASES OF ANIMALS.

SEVERAL species of mammals which have become domesticated are subject to pock-like diseases, and these affections in general are designated as animal pox.

Among these diverse forms of animal pox, that of cattle (cow-pox or vaccinia) is the most important from a medical standpoint on account of its known relation to vaccination.

In spite of the exceptional importance of vaccination in practical medicine, it must nevertheless be scientifically studied in connection with the remaining pock diseases, in which group it forms an individual species. The protection afforded by vaccination also finds a still more general elucidation if we extend our consideration to the other varieties of pox in the lower animals, or at least to the more important members of the group. It consequently seems necessary from both standpoints to give a brief description of the pock diseases of animals in general.

According to their general clinical character the different species of pox, including human variola, may be divided into two large and distinct groups (Bollinger). The first group, of which human pox (variola) serves as a paradigm, or example, represents actual pestilences which visit the particular species in question (man) as an epidemic, the other species (animals) as an epizootic, and which are capable of transmission throughout that species by means of both a fixed and still more a volatile contagium. The second group, on the contrary, does not exhibit this epidemic character; they are always of sporadic occurrence, and spread but slowly from individual to individual under the most favorable circumstances, since their further transmission within and outside of the species is due solely to a fixed contagium. In addition to human variola, sheep-pox, or ovinia (variolæ ovinæ), belongs to the pock diseases of the first group; horse-pox (variolæ equinæ) and the disease of special interest, cowpox, or vaccinia (variolæ vaccinæ), belong to the second group.

Further differences between the pock diseases of the first and second group are that the individual members of the epidemic group (variola, ovinia) run their course in their own species as severe febrile diseases, and that they are generally accompanied by a diffuse erup-

tion of pocks over the entire body. In the second group, equinia (variolæ equinæ; German, *Mauke*), however, the general symptoms are only slightly marked in the individuals of the species, and the generalized exanthem in particular is wanting. There is simply a local eruption, and this occurs only through inoculation at points where the fixed contagium has lodged and found an opportunity to force its way into the deeper layers of the epidermis through an injured place in the horny layer.

Having disposed of these general facts, the special data concerning these pock diseases in animals (sheep-pox on the one hand, horse-pox and cow-pox on the other) may now be considered. These facts have reference, first of all, to the clinical phenomena observed in the affected animals themselves, and then to the question of the power of transmission of these forms of pox to individuals of other species. Sheep-pox, or ovinia (German, *Schafpocke;* French, *clavelée*), a pestilence very much dreaded by sheep-raisers, is a highly contagious epidemic disease of the ovine species which has a mortality of over 25% and which frequently permanently damages the surviving animals, especially in their woolly covering. After an incubation period of eight or ten days, the disease usually begins with marked febrile symptoms, which persist for several days. Upon the decline of the fever a papulovesicular eruption appears upon the entire surface of the body. The individual pocks undergo suppuration, and their cicatrization is responsible for the scars which cause permanent defects in the wool of the affected animal. The clinical resemblance to human variola is at once apparent, and it is not to be doubted that sheep-pox and variola are closely related to each other.

In spite of the similarity existing between the two diseases, however, sheep-pox is not identically the same affection as variola, since neither disease can be directly transmitted to the alternate species [man to sheep or sheep to man]. During an epizootic of sheep-pox no one has, as yet, observed that the volatile contagium of that disease has ever caused an epidemic of human variola, and, vice versâ, an epidemic of human variola has never been the demonstrable cause of an epizootic of sheep-pox. From these facts it is evident that the two affections are apparently similar and yet pathologically different species, one of which is peculiar to man and the other to the sheep. They may also run their courses side by side, each affection being entirely independent of the other. The volatile contagium of both diseases very readily transmits the affection within its own species, but not outside of it to the other species.

The goat, which is closely related to the sheep zoologically, is also susceptible to a certain extent to the volatile contagium of sheep-pox, and the sheep-pox contracted by the goat always progresses with high fever and general exanthem. The existence of an original goat-pox is extremely questionable; it is more than likely that the very rarely observed cases of goat-pox are nothing else than stray cases of sheep-pox (Bollinger).

Although the contagium of sheep-pox in its volatile form is not capable of transmission to man (or to any other species, except the goat), the disease has been frequently successfully transmitted by inoculation with a fixed contagium. The ovination of man is not easily accomplished, just as we have previously observed that there was considerable difficulty in performing variolation successfully in the sheep. In the first decade of the nineteenth century Sacco and Legni were successful in producing ovination in man, and at a later date others were likewise fortunate, in isolated cases at least. It is nevertheless much easier to successfully inoculate sheep-pox into certain other animals, especially into cattle (Reiter) and into rabbits (Gerlach). It is important to note that in all of these successful transmissions of sheep-pox to other species, and especially to man, the inoculated disease has, without exception, been characterized by nothing but a local eruption resembling vaccinia, and never by a general eruption. It is consequently interesting and practically important to know that successful ovination, like vaccination and variolation, renders the inoculated individual, whether it be man or animal, immune to pock diseases in general (Sacco, Legni, and others). Ovination in man consequently confers protection against human variola

Reinoculation of the humanized or bovinized sheep-pox into sheep, or retro-ovination, is usually successful, and most frequently produces nothing but a local eruption, which nevertheless affords protection to the sheep against sheep-pox and other varieties of pox. The suggestion of Bohn to protect sheep from the natural sheep-pox by inoculating them with a modified ovine virus obtained from man, cattle, or rabbits is deserving of careful consideration.

In reference to the forms of pox occurring in the horse, the following facts are to be noted.

Both general and local eruptions of pocks are observed in the horse. The general eruptions are characterized by more violent general symptoms than are the local, but, in contrast to sheep-pox, they never assume an actual epizootic character. The nosologic position of horse-pox is still unsettled. It should nevertheless be

remembered that the direct injection of human variolous lymph into the circulation of the horse is said by Warlomont to produce a general eruption of pocks. When the contents of the pustules of horse-pox are inoculated into other species (man, sheep, cattle), they cause nothing but a local eruption, which looks like vaccinia and which also confers the same immunity upon the inoculated individual. The local form of horse-pox (German, *Mauke*) is known as "grease," and is of historic significance because Jenner erroneously regarded it as the actual parent of vaccinia on account of its local character. Equine variola (variolæ equinæ) appears in horses usually upon the fetlock-joints of the hind legs, and is introduced by an initial fever of three days' duration. The surrounding skin then shows marked inflammatory swelling and is surmounted by closely set vesicles, the contents of which are clear at first and clouded later. These pocks tend to rupture, partly spontaneously and partly as the result of traumatism, and are then transformed into superficial ulcers of irregular contour which heal slowly. The lymph of equine variola, which frequently (?) has an ammoniacal odor, is capable of further effective inoculation both in the horse itself and also in sheep, cattle, and man (equination); retro-equination in the horse from the ovine, bovine, or human species is equally easy of production. Such equinations or retro-equinations are usually followed by the appearance of large vesicles with well-marked outlines, completely resembling those of vaccinia and gifted with the same protective properties. It consequently happened that in former times when fitting opportunities presented themselves equination was frequently substituted for vaccination in the human species. This practice never became general, however, on account of the well-grounded fear that these prophylactic equinations might transmit other affections peculiar to horses—glanders in particular. In more modern times such equinations were no longer performed in man for prophylactic purposes.

In regard to the nosologic position of equine variola, all the more modern and competent investigators seem to agree that it is probably nothing else than a variola or a vaccinia which has strayed from the human or bovine into the equine species. This is not the place for the production of proofs supporting this view, since equination no longer has any actual importance in relation to the prophylaxis of variola.

Both theoretic and practical interest are therefore centered upon cow-pox or vaccinia. When the disease appears spontaneously in individuals of the bovine species, as it sometimes apparently does,

such cases are designated as original or natural vaccinia. Since this original vaccinia is the foundation for the entire procedure of vaccination, it certainly deserves a more detailed description than all other varieties of animal pox.

Natural vaccinia is not a particularly frequent disease, and seems to be even rarer at the present time than formerly. It is most frequently observed during the spring and early summer months, at which season the milk production of cattle is greater and at which time they are most frequently milked. It is without exception a localized and never a general form of pox, which is rarely observed in any but milch-cows, although it may occur primarily and secondarily in other individuals of the cattle family (heifers, calves, and bulls). Cow-pox is practically always confined to the actual milk sites; *i. e.,* not only the udders, but also about their bases. All these peculiarities of natural vaccinia make it extremely probable that the procedure of milking plays the most important rôle in the genesis of the disease, and that the further transmission of the fixed contagium from cow to cow is largely due to this manipulation.

The development of natural vaccinia may be preceded by general symptoms, such as diminished appetite and some fever, but this is not so in the great majority of cases. Small reddened areas, varying in size from that of a pea to that of a cent or halfpenny, are first observed upon the swollen and painful udder. These areas are transformed into firm papules, and are soon surmounted by vesicles which rapidly increase in size. The matured vesicles are multilocular, may or may not be umbilicated, and contain large quantities of a clear lymph. Toward the end of the first week the entire affected area becomes reddened and infiltrated and the contents of the vesicles become purulent. At about the twelfth day the vesicles commence to dry up. During the stage of suppuration there is frequently some fever, and other symptoms of a mild constitutional disturbance appear, while the secretion of milk is frequently markedly decreased. It is also worthy of note, in reference to the course of the disease in general, that in natural vaccinia the eruption of the individual pocks does not occur uniformly, but in successive crops, so that fresh and dried-up pustules may be observed side by side. This condition of affairs does not obtain in inoculated cow-pox, whether it be in man or cattle.

In an individual case there may be some minor deviation in the course of a natural vaccinia in the cow as just described, which are largely dependent upon intercurrent traumatisms. As a rule, how-

ever, the disease accurately follows this course and terminates after a duration of two and one-half or three weeks. After the separation of the crusts, shallow round or oval scars remain at the site of the pocks upon the udder, and these scars are frequently visible after the lapse of years.

To the best of our knowledge, natural vaccinia attacks a cow once only during its lifetime, and the same peculiarity is characteristic of inoculated vaccinia. Since we know of no authentic case of an animal showing a susceptibility to repeated vaccinations or suffering from repeated attacks of cow-pox, it would seem that the immunity conferred upon cattle by an attack of the disease is a permanent one. In the section upon "Revaccination" it will be pointed out that the immunity in the human individual, on the contrary, lasts only for a certain number of years. Vaccinia is easily transmitted to the human individual by virtue of its fixed contagium, and the humanized disease may be further inoculated from individual to individual with still greater facility. Unintentional transmissions of vaccinia to man occurred frequently in former times, and are still occasionally observed at the present day. The manipulation of milking cows affected with cow-pox was always the most common and productive cause of this accidental transference of the vaccine virus to the human individual. The pocks of accidentally acquired vaccinia naturally occurred most frequently upon the hands of milkmaids, and the country-folk were not slow to note the resemblance of this exanthem to that of the eruption upon the cow's udder. From repeated observation, they were equally impressed with the fact that such naturally vaccinated individuals usually remained immune throughout subsequent epidemics of smallpox. This cardinal fact is of historic interest, as it formed the starting-point for the theory of vaccination and the great agitation that followed upon the introduction of the procedure.

The fixed contagium of vaccinia, moreover, is capable of accidental transmission and intentional inoculation not only in cattle and man, but also in the horse, sheep, goat, and some other species. With one exception, presently to be mentioned, the effect of every such vaccination in man or animal is always the same—namely, the appearance of a vesiculopustule, at the point of introduction of the virus, resembling the lesion of variola, and with the disappearance of this lesion the vaccinia terminates. The sheep alone responds to vaccination with bovine virus in a most striking manner, sometimes developing not only local pustules, but also a subsequent general

eruption over the remaining surface of the body resembling sheep-pox (Wolff, Koch, Fürstenberg). Under certain conditions the sheep is said to also possess the remarkable power of transforming the fixed contagium of vaccinia into a volatile one, and in this manner the animal is enabled to cause a spread of the disease throughout its own species (Bollinger). For these reasons the vaccination of sheep as a prophylactic measure against sheep-pox has been generally abandoned. (The effect of inoculating sheep with humanized or bovinized sheep-pox is quite different, and has been previously considered.)

We have already mentioned and considered in detail the fact that cattle are readily inoculated, not only with humanized vaccinia and human variola, but also with sheep-pox and horse-pox. The only reaction to all these procedures is, without exception, the pro-duction of a local pustular eruption, which, when inoculated back into the original animal, likewise causes nothing but a local affection capable of further cultivation throughout the species. Finally, the temporary or permanent protection conferred upon individuals of any species (human or animal) by successful inoculation with any of these varieties of virus extends to all forms of smallpox, whether they be animal or human.

If all these facts are considered together, the practically important conclusion is reached that the organism of the cow possesses, to a most marked extent, the property of transforming generalized small-pox such as variola and sheep-pox into a localized form, and that, although it mitigates the severity of the disease, it does not prejudice the immunizing effects. The practical application to human variola furnishes the most important example of this property, and has been fully considered in the preceding section, upon the Variolation of Animals.

The question as to the real nature of vaccinia has already been touched upon and some indication has been given of the still prevalent controversy upon the subject. The importance of this matter makes it necessary to return to this controversy and approach the question from a somewhat different standpoint. There have been two factions in this discussion. The one, composed particularly of French in-vestigators (Layet and others), and headed by Chauveau, regard both bovine and humanized vaccinia as an independent form of pox, originally different from human variola, and claim that it is a disease peculiar to the bovine species and analogous to the sheep-pox of sheep. The other faction, first led by Thiele and Ceely, and now

represented especially by Bollinger, L. Voigt, Eternod and Haccius, Fischer, Hime, L. Pfeiffer, and others, believe that vaccinia does not differ in its nature from variola, but that it is simply modified small-pox. Since it is so easy to transform variola into vaccinia by trans-ferring the affection to cattle, they regard both diseases as identical in their nature. Brief reflection will show that the application of these opposite theories to the cases of so-called original vaccinia in the cow is important as deciding the entire question. Any further discussion upon this subject must consequently take these cases and their natural occurrence into consideration.

All previous experience teaches that these so-called original cases of vaccinia in the cow are commonly of sporadic occurrence, being separated from each other by periods of years or by great distances; in other words, that one case is not continuous with another. This condition of affairs is thoroughly unintelligible and mysterious if we accept Chauveau's theory as to the specificity of vaccinia. On the other hand, it would seem very plausible, and at least logical, if we looked upon these so-called original cases of vaccinia as nothing other than accidental and occasional infections of the cow with a virus of some other form of pox which has its origin in some recognized source. According to Bollinger, we may presume that the possible sources of the virus in question have been the following:

1. The sources of former times, consisting chiefly of the epidemics and pandemics of human variola which were formerly of such frequent occurrence;

2. The source of modern times, consisting partly of the epidemics of human variola, which are unfortunately still prevalent to a certain extent, but chiefly to be found in the great number of cases of human vaccinia.

In addition to these two chief sources of this virus of so-called original vaccinia, both of which are furnished by man, we might add another:

3. All the varieties of pox found in the domestic animals (sheep, horse), with which the cow frequently comes in intimate contact.

Although the proof of the absolute correctness of the last-named conception cannot be adduced at the present time, it would seem to have more to recommend it than any of the other hypotheses, and consequently should be provisionally accepted as the best ex-planation of the pathogenesis and etiology of vaccinia. Considering all things, I do not hesitate to regard vaccinia in the great majority of cases as an affection derived from human variola, and consequently

believe that the exciting micro-organism will be found to be identical with that of variola or a modified form of the same. In the future, medical science must look to the exact parasitologic investigation of this subject for more complete and decisive results. In the present state of medical knowledge, this is as far as we may profitably pursue the discussion concerning the possible nature of vaccine virus and of vaccinia itself.

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VACCINATION IN MAN.

HISTORY.

The fact that the so-called original vaccinia (cow-pox) was capable of transmission to the human individual by contact, has been known for an indeterminable period of time. Long before the days of Jenner, it had been observed that individuals who had never had smallpox, but who had been accidentally infected with cow-pox (milkmaids especially), remained immune when subsequently exposed to variola. Alexander von Humboldt, for example, in referring to his travels in the Tropics (1803), says that since the earliest recollection of man certain tribes of Indian shepherds in the Mexican Cordilleras had been thoroughly convinced of the protective effect of vaccinia against variola; Brun makes a similar statement in reference to the clan of Elihats in Baluchistan (Kussmaul). The belief in the immunizing effect of cow-pox was also prevalent among the country-folk of Europe, and thoroughly rooted in certain parts, especially in the southern counties of England, in Holstein and Mecklenburg, and in Hanover and Saxony. Here and there physicians (Heim) had occasionally taken notice of this belief, and in individual instances (Sutton and Fewster) had even temporarily engaged in experimental work upon the subject. It has also been established that some actual vaccinations were performed by the laity, and that, too, before the time of Jenner, for the avowed purpose of protecting the vaccinated individual against a future variola.

As early as 1763 Heim learned from his father, a country clergyman of Saxe-Meiningen, that the milkmaids of the vicinity were thoroughly convinced of the prophylactic value of accidentally acquired cow-pox. Sutton and Fewster, two English physicians, had also heard that vaccinia would confer immunity against variola. To test this belief, they inoculated several individuals who had been infected with vaccinia with human smallpox (1778). These attempted variolations were not successful, and the proof was sufficient in their minds to confirm the popular belief. The results obtained by Sutton and Fewster unfortunately did not receive proper consideration in medical circles, and they themselves neglected to make further experiments upon the subject. Benjamin Jesty, a farmer of Gloucestershire, was in all probability the first person in Europe to vaccinate with bovine virus for prophylactic purposes. With confidence in his own immunity, which he attributed to a previous attack of vaccinia, he successfully inoculated his wife and two

sons with cow-pox in 1774, and thirty-eight years later, long after Jenner's publication had become the property of the civilized world, these three individuals were found to be still immune to an attempted inoculation with variola. Somewhat later than Jesty, Platt, a school-teacher at Starkendorf near Kiel, likewise vaccinated the two children of his land-lord with bovine virus to protect them from an existing epidemic of variola (1791). His reason for the procedure was based both upon the belief popular in his Saxon birthplace and also upon the local traditions of Holstein.

It is clear, from all that has been said, that the idea of protective vaccination did not, like Pallas Athene, spring from the brain of any one individual. Indisputable credit is nevertheless due to Edward Jenner (born 1749, died 1823), a practising physician of Berkeley in Gloucestershire, since he carefully tested the correctness of the popular belief in the protective value of vaccination for more than thirty years (commencing in 1768), and then absolutely proved the accuracy of this belief by the unequivocal results of his series of experiments. For this reason alone the name of Jenner deserves to be placed among those of the benefactors of the human race. He especially gave evidence of an actual creative initiative by the fact that he was the first to inoculate with the virus of humanized vaccinia, and in this manner he made possible for all time the general employ-ment of the protective agent. In the beginning, his own experiments did not differ from those of Sutton and Fewster, but they were more numerous and more accurate. He first attempted to inoculate with variola those individuals who had at some previous time passed through an accidental infection with cow-pox (16 cases in all). In every instance the attempted variolation was a complete failure, although in some of these individuals more than thirty years had elapsed since the attack of cow-pox. From these facts, which simply placed the knowledge previously gained by others upon a broader experi-mental basis, he now proceeded to an entirely new and independent line of experimentation. On May 14, 1796, he inoculated an eight-year-old boy (James Phipps) with virus obtained from a case of accident-ally acquired cow-pox in a milkmaid (Sarah Nilmes), and by this act accomplished the first vaccination upon a patient with a humanized vaccinia of the first generation. The boy developed a typical attack of cow-pox, just as though he had been accidentally infected with the natural bovine disease, and, as expected by Jenner, a subsequent variolation was followed by a completely negative result. It was thus definitely proved for the first time that, in one case at least, the humanized vaccinia was capable of further transmission in man,

and also that the humanized vaccine lymph possessed the same immunizing property against variola as did the natural virus. Jenner was by no means satisfied with this result, but waited for a further opportunity to repeat his experiment and to carry vaccination still further. Such an occasion did not present itself until two years later (1798), when he inoculated a boy with the bovine virus of a case of original vaccinia. The humanized vaccine from this boy was now successfully inoculated from individual to individual for 5 generations, and in all these cases subsequent variolations were followed by negative results. It was not until these facts had been obtained that Jenner gave to the world his memorable and epoch-making paper, "An Inquiry into the Causes and Effects of the Variolæ vaccinæ, known by the name of the Cow-pox (London, 1798)."

In this article, supported by his observations and experiments, he recommended vaccination as a sure and safe prophylactic measure against smallpox, in place of the inoculation of human variola, and showed that in the humanization of the natural lymph a means was furnished by which a necessary quantity of the effective vaccine virus could always be obtained.

Jenner's first publication excited an enormous amount of attention, and was soon translated into Latin as well as into all the European languages. This was followed in the next two years by two more articles, consisting chiefly of confirmatory and supplementary evidence: "Further Observations on the Variolæ vaccinæ or Cow-pox (London, 1799)" and "A continuation of Facts and Observations relative to the Variolæ vaccinæ or Cow-pox (London, 1800)."

In the mean time vaccination, in spite of considerable opposition in the beginning, had been very extensively tested and employed both in England and on the Continent. Many thousands of individuals were successfully vaccinated, and many hundreds were subsequently inoculated with variola as a control experiment. In all the vaccinated cases the variolation failed, and the claims made for the procedure by Jenner were consequently confirmed. After investigating the subject, the most noted physicians of the times, Pearson and Woodville in England, Aubert and Husson in France, Ferro and de Carro in Austria, Sacco of Milan, whose zeal excelled that of all others in Italy, Ballhorn and Stromeier of Hanover, and Sömmering and Lehr of Frankfurt-a.-M. in Germany, and Odier (Geneva) in Switzerland, declared themselves in favor of vaccination and issued the most convincing propaganda in favor of the procedure. The practice was also encouraged in the Netherlands, in Norway and

Sweden, in Russia, and in Spain and Portugal. In fact, before the new century had fairly commenced, vaccination was so inviting and apparently so effective a prophylactic against the dreaded epidemics of smallpox that it had the active support of the entire medical profession of Europe. In addition to the sanction of high medical authorities, there were other powerful factors that favored the spread of the procedure. Even among the laity there were deep-thinking and unprejudiced individuals in all countries who favored vaccination in their speech and writings, and thus gave the custom material support. It may thus be said without hesitation that the vaccination movement introduced by Jenner, universally began under the most favorable auspices, and that it rapidly spread throughout the entire world.

The extension of the movement found a visible expression in the foundation of public and private vaccination institutes. The first one of these was founded in London in 1799 by the friends of vaccination and placed under the direction of Pearson. Four years later, in 1803, there appeared the "Royal Institute for the Extermination of Smallpox," which Jenner himself personally conducted for many years. Both institutes did much to advance the cause of vaccination, since they carried out the procedure free of charge (on certain days of the week) and supplied lymph to their own and foreign countries. In Vienna, de Carro succeeded in having the "Imperial and Royal Institution for Foundlings" designated as the chief Vaccination Institute of the Austrian kingdom, and thus gave vaccination its first official recognition upon the Continent (1801). From its foundation this institution was most active in performing vaccinations, and by the careful, exemplary, and continuous cultivation of human lymph it furnished what is probably the most incontrovertible proof of the accuracy of Jenner's claims. In Berlin the Frederick William Orphan Asylum was fitted up in 1802 as a public vaccine station; in Breslau, Göttingen, and other German cities various similar public and private institutions sprang into existence between 1801 and 1805. The example of Austria was quickly followed by Russia (St. Petersburg, Moscow) and Italy (Milan), in which countries the lymph was in particular cultivated in the Foundling Institutes of the State.

The concrete characteristic of an actual prophylactic effect upon a large scale was a previously unheard-of decrease in the number of cases of variola and a great fall in the mortality from the disease in those regions where vaccination had been thoroughly carried out. This effect was already noticeable in the first decade of the nineteenth century; in the second decade it was still more marked; and subsequent years showed that the result obtained was a permanent one. At the same time, this result caused a number of governments to make vaccination an obligatory procedure for all their subjects. Bavaria

was the first State in which this occurred, since Reiter succeeded in having a Vaccination Law established in 1807 that was most exemplary in the majority of its details. According to this law, all children, without exception, were to be vaccinated in the first year of life, and it also contained a series of very precise and reasonable provisions in relation to the intelligent control of vaccination results, the keeping of records, compulsory vaccination during the existence of an epidemic of variola, and other important rules of conduct. The brilliant prophylactic results obtained by Bavaria, which were never excelled anywhere during the remainder of the century (v. Bulmerincq), were due entirely to the good points of this vaccination law. The action of Bavaria stimulated other States of the German Confederation to follow her example, and between 1815 and 1832 compulsory vaccination laws were enforced in Baden, Würtemberg, Oldenburg, Saxe-Gotha, Saxe-Meiningen, and Brunswick.

The conditions were less favorable under the two great German powers existing at that time (Austria and Prussia). Although steps were taken in Austria in 1801 to make vaccination indirectly compulsory, by requiring a certificate of vaccination upon entrance to any of the imperial schools, the law never passed beyond this point until 1886. In Prussia, the government contented itself with the annual encouragement of vaccination, and even this was not generally practised until 1810. Some years later (1816) a law for the entire Prussian kingdom was modeled after that of Austria, making vaccination indirectly compulsory, but this still left much to be desired.

The Scandinavian kingdoms (Sweden, Denmark, and Norway) were in hearty sympathy with vaccination, and soon most willingly accepted the procedure. Vaccination was introduced into Sweden in 1801, and after gaining considerable ground in consequence of the favorable results obtained, a law was passed requiring the universal performance of the procedure. The effect of this Vaccination Law in Sweden was a subsequent marked decrease in the mortality of variola, as is most definitely and clearly shown by a reference to the accurate mortality records of that country. This will be referred to later in detail in the section upon General Results of Vaccination and Revaccination. In Norway and in Denmark actual compulsory laws were not introduced, but both countries simultaneously passed decrees (1810) containing regulations that indirectly favored vaccination, and these were so rigidly enforced that they almost approached the law of Sweden and operated in a similarly advantageous manner.

In the United Kingdom (Great Britain and Ireland) the outlook

was anything but hopeful for a considerable period of time. In England especially, the cradle of vaccination, the procedure first seemed to flourish, but soon encountered all sorts of obstacles which were largely of a political nature. It was especially the character-istic aversion of the English people to any encroachment upon the national principle of "habeas corpus" that for a long time absolutely blocked any legislation upon the subject. An unsuccessful attempt to pass a vaccination law was made in 1853, but it was only after passing through the sad experience of repeated epidemics that the English Parliament finally passed the "Vaccination Act" in 1867, requiring the compulsory vaccination of children. The "Vaccination Act" was amended in 1871 for the purpose of increasing its efficiency, but the amendment was not so productive of the expected good results as might have been desired. In Scotland, legislative action was better and more prompt, since vaccination was made compulsory in 1864. The law was also much more systematically carried out in that country, and the prophylactic results were correspondingly more favorable. What has been said of England is equally true of Ireland, which received its Vaccination Law first in 1868.

In Italy vaccination soon met with great approbation. Jenner found no more inspired and independent fellow-worker in his own epoch-making labors than Luigi Sacco, a physician of Milan, whose name must be placed alongside of Jenner's in the history of vaccina-tion, and who in some respects even excelled the founder of the procedure. Sacco, who had never had variola when Jenner's first publication appeared, successfully vaccinated himself in 1799, and then allowed himself to be inoculated with variola. The result was negative, and having proved the prophylactic value of Jenner's method in his own person, he worked unceasingly on behalf of the procedure during the remainder of his life. His energetic work, chiefly directed to the extirpation of the general susceptibility to variola, was soon supported by the existing republican government of his country and by some of his colleagues (Moreschi in Genoa and Scassi in Venice). Even in the first years of his beneficent activity he was repeatedly successful, both in rapidly checking existing epidemics of smallpox in Italy by great numbers of vaccinations among the affected population, and also in nipping commencing epidemics in the bud by the same procedure. It was largely due to his efforts that his countrymen acquired a great confidence in the method. The force of his personality and of his will made vaccina-tion so popular within a short period of eight years that a great portion

of the population had voluntarily adopted the procedure as a family custom. This universal popularity was also maintained in later times, but the legal introduction of vaccination as an obligatory precautionary measure is still wanting in Italy at the present day.

A further and likewise very important service rendered by L. Sacco to vaccination lies, however, in the domain of pure science. He it was who, by numerous experiments, laid the most important foundation for the nosologic position of the vaccine process among the pock diseases (human and animal) in general. By transplanting vaccinia to other species,—to the sheep, for example,—and no less by inoculating men and cattle with equine and ovine variola, and by successful retro-inoculation into susceptible individuals of the same species, he was the first to clear the way for the comprehensive results obtained in the important and interesting domain of comparative pathology. He especially taught, by numerous experiments which he cleverly varied, the peculiar relations of all different forms and varieties of pox, as well as the grade of protection which they reciprocally afforded against each other, and he did this so thoroughly that all subsequent work in this field has been but supplementary to his own. We may consequently say, without fear of exaggeration, that Sacco made the profoundest impression upon the subsequent history of vaccination.

The unusual zeal with which vaccination was received in Italy from the very beginning was productive of good results in a third direction, although this was not due to Sacco himself. Many improvements were made in the technique of vaccination, chiefly consisting of the production of a most unobjectionable vaccine virus and of its further solicitous cultivation. Italy, in a word, became the cradle of pure animal vaccination, or that form of vaccination which is deservedly the most popular at the present time. After this method had been temporarily tried by Galbiati and Feola, it was brought to a high grade of technical perfection by Negri, of Naples (1849). Pure bovine vaccination—*i. e.*, the employment of a vaccine virus that has been obtained from a case of original cow-pox and artificially transmitted from cow to cow—is consequently still known to many by the historic name of the "Neapolitan Method."

In the Netherlands (the Holland and Belgium of to-day), as in Italy, vaccination not only met with a friendly greeting, but also became popular within a short period of time; without prejudice to the further extension of the procedure, there has never been a compulsory vaccination law in either country.

The impression made by Jenner's publication was far less lasting in France. It is true that the republican government was in hearty sympathy with the movement, and the same may be said of the subsequent First Empire, which even passed a formal decree favoring vaccination (1809). This decree, however, contained nothing but vague superficial requirements, and its application fell into lamentable disuse some years later under the Bourbon restoration. The revolution of July (1830), with its political consequence, the "Kingdom of the People," was productive of no energetic change, and matters were not improved by the Second Republic, the Second Empire, or the present existing republican government. France has severely atoned for this laxness in the practical application of vaccination by particularly numerous and malignant epidemics of smallpox in the course of the nineteenth century. This was not for want of warning, for the most distinguished men (Robert, Bousquet, Trousseau, and others) repeatedly raised their voices in warning against the existing laxity in this respect, but they were not accorded the necessary approbation from the responsible authorities. In the realm of pure science, on the contrary, France has shown a most commendable activity in the experimental work of the Commission of Lyons (1865) upon the vaccination question and in the subsequent publications of Chauveau. These experiments were made for the purpose of determining the nature of vaccinia and its nosologic relation to variola, and at the present time it must be admitted that the results obtained seem to be most questionable, if not absolutely incorrect.

Vaccination, in the full sense of the word, has never prospered any better in Russia than it has in France. The vaccination movement reached the former country in 1801 and received the sanction of the highest authorities. The services of the Foundling Asylums were invoked and the general introduction of the procedure was considered in 1802, but the execution of this well-intended plan was frustrated by the great extent of the Russian empire and by the injudicious selection of the individuals who were to carry out the method. Although the inoculation of cow-pox was rapidly disseminated in the larger Russian cities and permanently adopted by the higher classes of Russian society, the procedure has always been most deficiently carried out among the country population. In fact, this deficiency has been still more marked of late, since the abolition of serfdom has exempted the landlords from even an apparent interest in the vaccination of their dependents.

In Spain and Portugal vaccination was soon introduced from

France and England, and although the procedure was carried out on no small scale, the number of vaccinations has never been above the average.

There is not much to be said concerning the reception of vaccination by the more important countries outside of Europe. The conduct of the English, French, and Danish colonies was largely dependent upon that of their respective mother-countries. Vaccination reached the United States of America very early (1800) from England, and became disseminated to a considerable extent, although the procedure never became compulsory. The practice was imported into Mohammedan countries from Europe, and at first seemed to meet with approval, but vaccination never gained a strong foothold, and in the great majority of instances rapidly fell into disuse (Pollack).

The preceding synopsis shows how Jenner's discovery was received by the different nations and peoples, and how they subsequently supported the vaccination movement. It is to be specially noted that the original enthusiasm was not equally maintained in all parts of the world, and that in certain most important countries (England, France, and Russia) the first excitement was followed by a very marked apathy. Even in those countries where compulsory vaccination seemed to be strictly required by law, with several brilliant exceptions (Bavaria, Sweden), the subsequent practical application of the practice left much to be desired.

In many countries the vaccination movement advanced but slowly, while in others it suffered an actual retrogression. The causes for this condition of affairs varied to a certain extent with the particular people in question—sometimes it was due to disfavor or misunderstanding on the part of the ruling political power; sometimes, on the other hand, the lack of energetic leaders was responsible; but the best explanation of all was to be found in certain defects of the procedure itself. The first disturbing factor was the gradual discovery that the immunity, which had been so enthusiastically heralded by Jenner and his fellow-laborers, was by no means a permanent one. The number of cases in which successfully vaccinated individuals subsequently contracted smallpox during exposure to an epidemic increased slowly at first, and then more rapidly during the second decade of the nineteenth century. Although the original faith in the perennial character of the protection afforded by vaccination was maintained for some years, it gradually became clear to reasoning minds that a single vaccination could not be depended upon for a permanent prophylactic effect. The validity of the entire

procedure soon became questioned, not only in England, Jenner's native land, but also in France, Germany, and other lands; and many friends of vaccination either became disaffected or converted into direct antagonists of the prophylactic measure. Other light-hearted individuals comforted themselves with the fact that the absolute number of cases of smallpox in vaccinated individuals was notoriously less than among the unvaccinated, and found special satisfaction in observing that the large majority of cases of varioloid ran a relatively mild course. This latter fact, however, led to a most deplorable error. Many were misled into the belief that these particular cases were not variola at all, but only a disease which simulated it, and against which vaccination had no influence what-ever. Although Thompson attempted to overthrow this erroneous belief, during a great epidemic in Edinburgh (1820), by proving the etiologic connection between these cases of varioloid and variola, a still more evident argument was needed.

Such an argument was furnished by the increased malignancy of the epidemics of smallpox during the third decade of the nineteenth century. The disease not only caused a far greater sacrifice of human life in general, but the difference in the mortality among the vac-cinated and among the non-vaccinated was less noticeable than formerly, since great numbers of vaccinated individuals were attacked by the severe and fatal forms of the disease. The false theory of the specificity of varioloid was consequently overthrown, as was also naturally the dubious postulate deduced therefrom, that vaccination protected against variola but not against varioloid.

The idea of revaccination had its birth at this troublous time, and was shortly afterward put into execution. This supplementary measure not only fulfilled all expectations, but gave fresh impetus to the vaccination movement. The effect would undoubtedly have been much greater if it had not been for the active and contem-poraneous spread of the anti-vaccination agitation, which repudiated the whole procedure (vaccination and revaccination) and declared the measure injurious to the common good. Although the greater portion of this agitation lacked positive foundation, it caused the greatest uneasiness of the public mind, and, even to the present day, this has not been completely effaced among a certain portion of the population.

These vague prejudices were also nourished by the occurrence of syphilis after vaccination, the appearance of this disease seeming to bear some relation to the prophylactic measure. These cases, which

had been previously observed, now became the subject of anxious
comment, and were of such a nature as to place the previously mis-
trusted method in the worst possible light.   When we recall the many
efforts that were made to make vaccination unpopular, and the
violent objections to the procedure, not only from a hygienic stand-
point, but also from religious, legal, and political motives, we are
surprised that the advance of the principle of vaccination was not
even still more impeded than was actually the case.   Vaccination
had less to contend with in those countries in which the procedure
had been compulsory, and most of these countries soon adopted the
practice of revaccination.   All those governments which made the
vaccination of children compulsory gradually introduced revaccina-
tion into their armies by requiring the vaccination of all recruits.
In fact, the latter precaution was unhesitatingly adopted by certain
countries, such as Prussia, which had never had a compulsory vac-
cination law.   (See later, under "Revaccination.")

It was nevertheless true that at this time no one was able to
pronounce a decided opinion as to whether vaccination was to be
regarded as an advantage or as a disadvantage to mankind, and this
most important question consequently hung in the balance.   Nearly
twenty years passed before such an opinion was obtained, and then it
was elicited in a most striking manner.   The apparent motive was
furnished by an unsuccessful attempt of the British Parliament to
make the vaccination of children compulsory in the United Kingdom.
This particular regulation was issued in 1853, but subsequently met
with violent opposition, both within the pale of Parliament itself and
from the general public opinion of the country.   Two years later
(1855) the "General Board of Health" decided to officially interrogate
the most prominent medical authorities of the entire world upon
certain chief points concerning vaccination.   The result of this action
was the most unique occurrence in the history of hygiene, and did
much to clear up the existing confusion upon the subject.

The General Board of Health framed 4 questions, which seemed
to them to exhaust all the essential points, and which were to be
answered with discretion.   The first and most important of these
was in reference to the cardinal point as to "whether there was any
doubt that a successful vaccination conferred protection against
natural smallpox in most cases and an almost absolute protection
against death from this disease?"   The second question desired to
know "whether it was to be believed or suspected that the lessened
susceptibility of vaccinated individuals to smallpox predisposed them

to other infectious diseases, such as scrofula or phthisis, and whether vaccination exercised any deleterious influence upon the general health?'' The third question was ''whether past experience had given cause to believe or suspect that syphilis, scrofula, and other constitutional diseases could be transmitted by the lymph of the true vesicle of Jenner, and that an educated physician could, by mistake, take another disease product from a vaccinated arm instead of vaccine lymph?'' The fourth question was an elaboration of the first, asking ''whether the general vaccination of children was to be recommended, with the exception of those cases in which some special contraindication existed?''

These questions were addressed to 542 medical authorities, including the vaccination specialists and medical societies of Europe, Asia, and America, and in the course of the two following years (1856–57), 542 replies were received—the most imposing collection of opinions that had ever been undertaken for the decision of a medical question! Statistics were also solicited from the governments of all the countries in which vaccination had been generally practised for a long time, and especially from those in which the procedure was under more strict legal control. This request of the General Board of Health was also responded to with a most agreeable readiness. In this manner a great number of official records and scientific opinions were collected, and these were combined into a '' Blue-Book'' in 1857 and laid before the British Parliament. This English ''Blue-Book of Vaccination'' is unquestionably the most notable accumulation of all the important facts about the procedure that had been observed and established during the first fifty years of its experience. From the overpowering weight of statistics and from the equally important scientific arguments, the contents of this blue-book possessed an inestimable value for the vaccination question. At the time of its appearance it was practically an ideal triumph of vaccination over its open and concealed opponents, and was aptly designated as ''the most brilliant monument to Edward Jenner himself.''

These were the words of Sir John Simon, the representative of the General Board of Health, when he addressed the Parliament and made known to them the results obtained. There were only two skeptical replies to the first inquiry; all the remaining authorities, 540 in number, answered the question unhesitatingly in the affirmative, and thus explicitly recognized the positive value of vaccination. The second question was answered by a universal negative. There was some diversity of opinion in reference to the third question

(the likelihood of transmitting syphilis, etc., by the act of vaccination), so that no more definite conclusion could be drawn than that the greatest care should be given to the condition of health of the individual from whom the virus was obtained. The fourth question was answered in the affirmative by all those who had similarly responded to the first. This was the summary of the greatest medical inquiry that the world had ever seen.

This report, nevertheless, had relatively little practical importance. In Great Britain and Ireland, the theoretic necessity of compulsory vaccination was frankly recognized, but the legal settlement of the matter was not accomplished for a number of years (Scotland, 1864; England, 1867–71; Ireland, 1868). In other countries the awakened interest was, if anything, still less marked, inasmuch as no energetic steps were taken in those places where they were most necessary. It is to be very much regretted that a most important question, that in reference to the desirability of, or necessity for, revaccination, was not included among those framed by the General Board of Health. This was largely due to the fact that the question of revaccination did not seem ripe for discussion at that time. The omission of this question was, nevertheless, a great error from a practical standpoint, for after the publication of the "Blue-Book," every attempted advance was hindered for this very reason, and it became evident that more fruitful work upon this particular point was necessary. This is why this triumph of vaccination was great in its conception, but meager and insufficient in its practical consequences.

The seventh decade of vaccination passed without any noteworthy occurrence, as the epidemics of variola in most of the European countries were only of moderate severity. Under these conditions the vaccination movement experienced no actual challenge, and in consequence again threatened to stagnate. In order to improve matters a severe but purifying outbreak was necessary, and this was furnished by the epidemic that made its appearance in Europe at the close of 1870. It seemed as though the old malicious fiend of smallpox wished to reveal himself openly to mankind and show them that he was far from being exterminated by blue-books alone and by the ingenious arguments of scientific authorities.

The violent pandemic of smallpox in the years 1870–73 exceeded all others in violence and extent. When viewed in the light of the world's history, this visitation seems to have been a Nemesis for the accumulated sins of omission of the European nations, but it also was

a warning that was not neglected.   It was largely due to the recently acquired fear of smallpox that a sanitary measure of the highest importance, the "Imperial Vaccination Law" of 1874, was framed by the young German empire.   At least one of the European powers, and the youngest at that, consequently proved the truth of the adage that necessity makes men not only wise, but also determined.

This pandemic began as an epidemic in western Europe in 1870, before the outbreak of the Franco-Prussian war, which so changed the political aspect of the country.   The disease became pandemic by its extension to the east, which was chiefly due to this war, inasmuch as the introduction of the contagium into Germany and Switzerland was greatly helped by the lodging of large numbers of French prisoners.   The disease soon raged furiously in the northern, southern, and extreme eastern portions of Europe, and it was not until 1873, a considerable time after the establishment of peace between the two contending nations, that the pandemic disappeared from the Continent.   Although the number of cases of smallpox, and especially the mortality, must seem very great when compared with the ordinary causes of death, the pandemic by no means attained the severity which has been recorded of the epidemics occurring in the pre-vaccination era.   This was particularly true in those countries in which vaccination had not been absolutely neglected, but in which more or less stringent regulations in reference to vaccination and revaccination had been enforced for a considerable time.   A notable example was furnished by the troops of the German army, in which the number of individuals attacked and the mortality of the disease were markedly less than among the remaining population of the Continent.

The greater portion of the soldiers of the German army had been vaccinated in their childhood, and at least all of them upon entering the service, since the vaccination of recruits had been obligatory in all departments of the German army for quite a number of years.   In the French army, on the contrary, vaccination had been greatly neglected and revaccination was not practised at all.   This marked difference between the two opposing forces found a truly classic expression in the marked contrast offered by their relative susceptibilities.   The absolute mortality of the French was nearly 50 times greater than that of the Germans, and their ratio of deaths to the total number of cases was at least twice as great.   These facts proved that smallpox not only attacked and killed an incomparably greater number of soldiers in the French than in the German army, but that the disease also pursued a much more malignant course in the former body of men.

A very marked though less striking difference was observed in favor of the mortality from variola in the German army as compared with that of the civilian population of Germany.

The favorable results obtained in the German army by compulsory vaccination were collected, and upon them the medical profession based a demand for a general Vaccination Law, which was to be enforced throughout the newly constituted German empire, and which would place the principles of vaccination upon a firm and secure basis. The Königsberg "Verein für Heilkunde" made the first suggestion, since the plan proposed by some of its members (Möller, Bohn, Pinkus) fortunately met with approval, not only from the society itself, but also from the proper authorities elsewhere in the kingdom. This plan formed the foundation of the present "Imperial Vaccination Law" of Germany, which was approved by the Reichstag April 8, 1874, and which took effect April 1, 1875.

Both dates, and especially the latter, well deserve to be remembered in the history of vaccination, since they mark, for the German empire at least, the beginning of a new era in the prophylaxis of variola. It may be said without exaggeration, that by the application of this law, Germany made herself secure against the ever threatening and malicious fiend of smallpox.

The provisions of the German Vaccination Law may be briefly stated as follows (Bohn, Curschmann, Peiper):

Every child shall be vaccinated within the calendar year following that of its birth, provided it has not passed through an attack of natural variola. A non-vaccinated child, who according to medical testimony cannot be vaccinated within this time without endangering its life or health, is to be vaccinated within one year after the disappearance of the existing contraindication. Every pupil in public or private schools is to be revaccinated when twelve years of age, if he has not had smallpox within the previous five years. If the revaccination is unsuccessful, it is to be repeated in the following year. In addition to vaccine physicians, there shall be physicians authorized by the government for the exclusive purpose of performing vaccination, and the procedure shall be carried out free of charge. Every vaccinated individual must be presented to the physician who vaccinated him, not earlier than the sixth or later than the eighth day after the vaccination, for the purpose of determining the result; the vaccine physician must keep accurate records of the results he obtains, and these are to be annually forwarded to the authorities. Upon official demand, parents, foster-parents, and guardians are required to produce a medical certificate as proof that the vaccination of their children, or of children committed to their care, has been performed at the proper time or that legal grounds exist for its omission.

The subsequent paragraphs of the German Vaccination Law refer to the formation of vaccine districts in the individual States of the empire, to the appointment of vaccine physicians, and to the establishment of vaccine stations. The various governments were also instructed to provide for the erection of a certain number of State institutions for the production of a good vaccine lymph.

The law originally allowed the use of human vaccine lymph, lymph from an original vaccinia, and bovine lymph from an artificially transmitted vaccinia. When serious objection was urged to human lymph and retro-vaccine lymph (*i. e.*, the possibility of transmitting syphilis), it was subsequently (1885) decided to gradually adopt the use of pure animal lymph as rapidly as the State institutions could furnish the necessary quantity of the pure animal virus. Since the latter requirement has been fulfilled, the legitimate and regular form of vaccination in the German empire to-day is pure animal vaccination (and revaccination).

The approval of the Vaccination Law by the German Reichstag was by no means unanimous, for many of the members were opposed to the measure for judicial reasons or from hygienic scruples. Some regarded the introduction of compulsory vaccination and revaccination as an inadmissible attack upon the personal liberty of the individual; others, as might have been expected from previous experiences, maintained that personal health might possibly be damaged. Repeated petitions and proposals were subsequently addressed to the Reichstag by the opponents of vaccination, more or less violently demanding the repeal of the existing vaccination law. The German Reichstag has, in this respect at least, fortunately proved itself worthy of its high mission, for, up to the present time, all these propositions have been defeated by a large majority.

In the mean time the German people have had no cause to complain of the effects of this law, since the results of compulsory vaccination and revaccination in all parts of the empire have undoubtedly been extremely good. During the last twenty years smallpox upon German soil has become more and more of an exotic growth, inasmuch as the personal susceptibility to variola, in the most outlying population, has been reduced to a minimum and the opportunity of acquiring smallpox is of rare occurrence in the central portion of the country. During the new vaccination era in Germany cases of smallpox have occasionally been observed upon its exposed frontiers, and have been due to the introduction of the disease from without. There has been no great epidemic of variola in Germany since 1875.

It might have been supposed that European countries generally would have either followed the good example of Germany or have

been stimulated to the production of still better legislation. Nothing of this kind has occurred, however, and at the present time Germany alone enjoys comparative immunity from variola. In other European countries, with few exceptions, the vaccination requirements remain about the same as before, and the best of them are inferior to those of the German law. As might have been expected, these countries have not experienced an abatement of smallpox to the same degree as has been observed in Germany. The appeal of the International Medical Congress at Turin (1880) to all the States and governments of Europe to make vaccination at least generally obligatory fell upon deaf ears, and but few advances in legislation have since been made (Austro-Hungary). In Switzerland the legislation has even been of a retrograde character.

In Austria, at the present time, vaccination is still only indirectly compulsory so far as the entire civil population is concerned; it has only recently (1886) been decided to insist upon the vaccination of recruits in the army. In Hungary, on the contrary, a vaccination law was passed in 1887 which most nearly approached that of Germany, and yet the requirements were by no means so precise. In 1882 the Medical Commissioners of Switzerland proposed a plan of vaccination and revaccination directly modeled after that of Germany, and laid it before the Bundesrath. This plan met with great disapproval (May, 1882), which was further manifested by a retrograde vaccination movement in those cantons which had formerly enjoyed rigid vaccination regulations. The Canton of Basle, for example, which had adopted a fairly strict vaccination law in 1875, now repealed the same by popular vote and did away with every form of compulsory vaccination. The sum total of this and other attempts has caused a more or less increasing neglect of vaccination all over Switzerland, in spite of the appearance of subsequent epidemics.

The remaining European countries have simply continued the previously existing regulations in regard to vaccination; none of them, with the exception of Germany, has as yet proposed the introduction of an obligatory revaccination law to apply to the entire civil population.

In the preceding sketch an endeavor has been made to outline the more important features of the history of vaccination. Were we to dwell further upon these details, we should be forced to trespass beyond the limits of this work. Certain historic facts concerning revaccination and the anti-vaccination movement will be added later at an appropriate place. What has already been said is certainly sufficient to give an approximate representation of the spread of the vaccination movement throughout Europe and America.

The picture as we see it to-day is by no means encouraging in all of its details, and portions of it must cause a deep sense of regret. It consequently remains as the task of future generations to brighten up these dark spots and make the picture a brilliant and harmonious whole.

LITERATURE.

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THE HYGIENE AND TECHNIQUE OF VACCINATION.

The employment of a faultless vaccine virus in every case is necessary for the correct and safe performance of vaccination. A vaccine virus may be said to be faultless when it contains a sufficient quantity of the effective principle of vaccinia free from all contamination. It is possible to obtain such a virus only by the observance of certain indispensable precautions.

In the first place, the vaccine virus must be obtained only from those well-developed typical vaccine pocks which are still in the vesicular stage of their development and whose contents are therefore clear and not yet purulent. The employment of the contents of vesicles which have already become purulent, or even of dried vaccinia scabs, although frequently practised formerly, is no longer admissible. This is partly due to the great uncertainty of the specific result, but more particularly to the danger of mixed infection.

In the second place, the condition of health of the individual (human or animal) from whom the vaccine virus is obtained must be above all suspicion. This is a very necessary safeguard, since it prevents the inoculation of other pathogenic entities which thrive under the same conditions as does the effective principle of vaccinia, and which might injure the health of the vaccinated individual. The condition of health of the individual furnishing the virus can be regarded as perfect only when his own general health is good; when he possesses no diseased antecedents; and when his immediate ancestors have neither symptoms of disease nor questionable medical histories. Such conditions are most easily obtained in young individuals with vaccinia, and it is consequently the custom to obtain

vaccine virus only from children or from calves or heifers. Since the purity of the vaccine virus is a circumstance of the greatest hygienic importance, it is consequently the duty of the vaccine physician to always procure a sufficient guarantee (private or official) as to its quality.

The removal and preservation of the vaccine virus also requires certain technicalities and precautions which are necessary to protect it from immediate contamination, from rapid decomposition, and from subsequent deterioration.

Genuine vaccine material, obtained directly from cases of vaccinia, is at the present time employed in two different forms—as lymph and as the so-called pulp. Lymph is the older form and that one which has been employed for a long time; pulp is a more recently obtained material. By lymph, we mean only the clear and fluid contents which are found in the well-developed vesicles of vaccinia; by pulp, on the contrary, we mean this clear fluid together with the specifically infected epidermic base and with the specifically infected epidermic framework of such a vaccinal pock. Nothing but lymph is taken from the human vaccinal pocks, in order to save the individual (child) as much as possible. In animals, however, the pulp is much to be preferred to the lymph, since a greater amount of material may be thus obtained. All the evidence indicates that animal pulp is more likely to produce vaccinia than animal lymph, since it contains the effective principle of the disease in a much more concentrated form.

In order to obtain lymph, the fully developed vaccine vesicles are incised in a radiating manner, by means of a small sterile lancet, and the clear contents of the individual loculi are allowed to flow out. If the lymph is not to be immediately employed for vaccination purposes, it may be preserved by allowing it to dry upon small sterile strips of ivory, fishbone, or horn, or between two carefully cleansed glass plates. It is still better, however, to preserve it in a fluid condition in sterile capillary tubes or gram bulbs, and then it is advisable to add a certain amount of glycerin, which aids in the preservation and increases the volume of the virus. Lymph may be diluted with three or four times its volume of pure glycerin or with the same amount of a mixture of equal parts of glycerin and water. This dilution markedly increases the durability of the lymph and does not sacrifice any of its effectiveness. This glycerin lymph, when sealed up in gram bulbs, packed in cotton, and kept in a cool place, usually remains unchanged for months, and is the most convenient form in which vaccine lymph may be preserved at the present time.

In order to obtain pulp, a vaccine vesicle (of an animal) is scraped away from the underlying papillæ of the corium by means of a spatula or spoon-like instrument. The vesicle is to be removed unopened and entire, together with its base of epidermis (the rete Malpighii), and the production of any hemorrhage should be carefully avoided. The partly fluid and partly solid mass so obtained is now rubbed up into an emulsion with a small amount of glycerin (vaccine emulsion). This emulsion is then preserved in gram bulbs under the same precautions as are observed in the case of lymph.

The ordinary humanized vaccine lymph is a clear, somewhat sticky fluid of a light yellowish color, and when examined microscopically, is always found to contain certain elementary constituents. Very fine fibrinous coagula, a moderate number of leucocytes, and a few isolated red blood-corpuscles may be discerned without difficulty. When viewed under higher powers, rather numerous corpuscular elements are observed, which are very small and particularly characterized by their sharply outlined edges (Chauveau). These corpuscles, which are also found in human variolous lymph, approximately resemble the spores of the *Cytorrhyctes variolæ* (L. Pfeiffer), and are probably identical with them. (See "Variola," under Etiology, on p. 35; also the observations concerning Buttersack's threads and spores, on p. 34.) The animal vaccine lymph is thicker and still more sticky than the humanized form and contains the same elements.

The genuine animal vaccine pulp, on the contrary, is a gray or reddish-gray mass, which upon microscopic examination is found to contain a large number of red blood-corpuscles in addition to the constituents of the lymph. Elements of the rete Malpighii and prickle cells, with their peculiar degenerative forms, horny cells, and masses of detritus are also present in large amount.

The species of the individual furnishing the vaccine material determines not only the choice of the form of that material (pulp or lymph), but also the time at which it is to be procured. This time naturally depends upon the number of days required for the vaccine vesicles to reach the stage of full development, and this period is different in the human and bovine species. The vaccine vesicles reach the acme of their development quicker in cattle than in man, and since it is not allowable to wait for the purulent transformation of the contents of the vesicles, it follows that the animal vaccine material (pulp or lymph) must be obtained at an earlier date than the humanized virus (lymph). In a general way, the fourth or fifth

day may be designated as the appropriate time for harvesting the animal vaccine material, while the human vesicles are not usually mature until the end of the first week. It should be incidentally remembered that the period of maturation of the humanized vaccinia and the particular time for the removal of the lymph from the human vesicle thoroughly agree with the empiric data handed down to us in reference to procuring variolous lymph for the purpose of inoculation.

Further differences between human and bovine vaccine material are to be found in their relative advantages and disadvantages and in the dangers attendant upon the employment of either form. It will be better to first consider the human vaccine material (or the so-called child-lymph), since Jenner's recommendation caused its exclusive use for a long time, and it is still very commonly employed at the present day.

The great advantage which child-lymph (or human lymph) possesses over animal vaccine material is that it may always be easily obtained without special difficulty or expense wherever vaccination has once been generally introduced. Vaccination would have experienced much greater difficulties in so rapidly and so universally assuming its historic place as a prophylactic measure against smallpox had it not been for Jenner's great personal service in first testing and then recommending human lymph as a most practical vaccine material. This peculiarity of human vaccination, which is particularly striking in the direct vaccination from arm to arm, is also combined with a further advantage—the possibility of carrying out the elementary principles of asepsis much more satisfactorily than can be accomplished in animal vaccination. A healthy child, freshly washed and clothed in spotless linen, is always a cleaner individual than any calf or heifer, entirely disregarding the fact that the idea is not so repulsive to the lay mind. It is also true that of all vaccine materials the child-lymph is the surest, not only to "take," but also to produce a regular and mild form of the disease in the vaccinated individual. The latter qualities are particularly noticeable when the human vaccine material has been thoroughly humanized; *i. e.*, when the vaccine virus has passed continuously through quite a number of children. The human lymph is also more constant than the animal vaccine material, since it may be preserved for a considerably longer time, either pure or mixed with glycerin, without spoiling or losing any of its specific potency.

In contrast to all these advantages of human vaccine material and its employment in the form of human vaccination, there are

certain supposed and actual disadvantages to be considered. It has been claimed that the cultivation of vaccinia exclusively in the human species causes the vaccine material to degenerate in time, so that the disease commences to run an abortive course and becomes more and more impotent. This is no reproach to humanized vaccinia, since the same condition of affairs is observed in vaccinia cultivated exclusively in animals of the same species. Experiments have frequently been made in which vaccinia has been continuously inoculated from one individual of the bovine species to another, and it usually happened sooner or later that the disease deteriorated and could be restored to its original condition only by inoculating it into an individual of some other species. There is consequently no reason for saying that the gradual deterioration of the genitures is peculiar to humanized vaccinia. At the present day it is no longer believed that humanized vaccinia is inferior to animalized vaccinia in this respect.

The reason for this loss of strength of the genitures (animal or human) has not yet been sufficiently explained; the fact itself is, however, frankly admitted by all experienced vaccine physicians.

A further and much more weighty objection to the employment of human lymph is the possibility of transmitting contagious diseases, particularly syphilis, by the act of vaccination. The possibility of this occurrence must be unquestionably admitted, since the history of vaccination has furnished a series of concrete facts which amount to the most positive proof. It is equally true, upon the other hand, that syphilis is not capable of transmission by bovine material, since it is impossible to infect cattle with syphilis. This is the most important advantage which animal vaccination possesses over the humanized virus, and, in the eyes of many, it is sufficient to prove the absolute superiority of bovine vaccine material. It should nevertheless be particularly noted that every case of vaccine syphilis naturally excites a great deal of attention, and that, on the whole, they are nevertheless very rare in comparison to the many million human vaccinations that have been made in the past. It may also be added that every outbreak of syphilis after vaccination does not deserve the name of vaccine syphilis, since in some of these cases it is either certain or highly probable that the individual was previously infected with syphilis (especially children with hereditary syphilis) and the disease simply manifested itself at the site of the vaccination. It is clear that cases of this character should not be looked upon as the result of vaccination, and they consequently

require no further discussion. The question whether the use of humanized lymph is admissible depends more particularly upon those cases which from their pathogenesis must be designated as true instances of vaccine syphilis.

Since the possibility of the transmission of syphilis has been scientifically proved, these cases practically belong to the group of avoidable medical errors. They should therefore not be used as a reproach to human vaccine material, especially since the carelessness in these cases has been of the grossest nature. It is certainly contradictory to the most elementary ideas of medical caution to employ human lymph from a child who is open to the slightest suspicion of having hereditary or acquired syphilis. It is but just that the cases of actual vaccine syphilis should usually be directly referred to the carelessness of the physician who vaccinated.

Since vaccine syphilis will be more fully considered among the complications of the course of vaccination, these remarks will suffice for the present. It is clear from what has been said that the chief objection to human vaccine material, the possibility of the transmission of syphilis, practically amounts to almost nothing if the physician who vaccinates carefully and conscientiously observes all necessary precautions in obtaining human lymph. I am consequently not yet able to unreservedly agree with all those who look upon the general introduction of animal vaccination as the only salvation of the entire procedure, and who have been carried away by their enthusiasm over this one advantage of animal vaccine material. In my opinion, the historic rights and actual advantages of human vaccination are great enough to allow the choice of the particular vaccine material to be employed in any given case to be dependent upon the special existing conditions. It is also my conviction that human vaccination still possesses a certain justification in comparison with the employment of animal vaccine material.

What has been said of syphilis is equally true of other infectious diseases which are found exclusively in the human species (such as leprosy), and which might possibly be transmitted from the person furnishing the vaccine lymph to the vaccinated individual. Those infectious processes which are equally common in cattle and in man (such as tuberculosis) have evidently no bearing whatever upon the question of the superiority of the animal vaccine material over human lymph [unless Koch's view that *Perlsucht*, or animal tuberculosis, is not communicable to man should prove to be correct].

Since the danger of vaccine syphilis from the use of human lymph has been greatly magnified by the opponents of vaccination, animal

vaccine material has been perfected in recent years as a concession to this opposition, and especially in the interest of the extension of the vaccination movement. It was desired to take away from the opposition the only plausible objection that they had been able to produce, and at the same time to give the friends of vaccination the moral support of feeling that their battle was being fought with a faultless weapon. The idea was a worthy one in every respect; it showed superior wisdom in yielding a subordinate point as well as a warm-hearted interest for the further growth of the entire principle. These efforts have been crowned with success, although a considerable time elapsed before it was possible to overcome the obstacles that interfered with the general employment of the animal vaccine matter. The introduction of animal pulp (or emulsion) in place of the previously employed vaccine lymph of calves and heifers marks a great advance in animal vaccination, since the likelihood of obtaining a successful result has been greatly increased. For many years human vaccination was greatly superior in this respect, but owing to the use of animal pulp this difference can hardly be said to exist at the present time.

The chief obstacle, however, and the one which continually prevented the rapid introduction of animal vaccination, was the difficulty, previously emphasized by Jenner, of obtaining a sufficient supply of the animal vaccine material. Original cow-pox, the natural source of vaccine virus, was never a common affection, and the discovery of a new case was always looked upon as a lucky accident. Institutions and appliances for the regular cultivation of animal vaccinia in the bovine species from such cases of cow-pox were entirely wanting for a number of years, and the technique of artificially producing fully developed vaccine vesicles in cattle was as yet unknown. Such knowledge was first obtained in the institutes of animal vaccination founded by those governments which possessed compulsory vaccination laws, and these institutes were gradually increased in size and number until they were able to produce sufficient animal vaccine material for the entire population. The German empire, which takes the lead of all the governments of the earth in everything pertaining to vaccination, has succeeded in passing a law that every vaccination and revaccination within its political boundaries shall be regularly performed with nothing but animal vaccine. (Resolution of the Imperial Vaccine Commission of 1884; approval of the resolution by the Bundesrath, 1885.)

The fame of having placed animal vaccination upon a firm foundation is due to Negri and his predecessors in Naples. The Neapolitan method was taken up later (in 1864) in Holland, and brought to a high degree of perfection. Among those who rendered great service in the introduction of the procedure may be mentioned Lanoix and Layet in France, Warlomont in Belgium, Haccius in Switzerland, and Pissen, L. Voigt, Fischer, L. Pfeiffer, L. Fürst, and others in Germany. Although the institutes for the production of animal vaccine material were originally of a private character, and are still so to the present day in certain countries (Holland, Belgium), the various governments gradually founded institutes of their own, which were increased in number as occasion demanded. It has thus become possible to supply at all times a uniform quality of vaccine material in sufficient quantities.

The special technique of the production of artificial animal vaccinia in young cattle can here be but very briefly gone into. The udder or the scrotum of the selected animal was formerly chosen as the site of the inoculation; at the present time the inferior abdominal region is preferred, since it is easier of access and more readily kept clean. The region between the navel and genitalia is first carefully shaved and then rendered as thoroughly aseptic as possible by means of soap, carbolic acid, and boiled water. A moderate number of punctures or incisions are now made and the vaccine material is applied. It has lately become customary to considerably increase the number of receptacles for the virus, since experience has shown that more vaccine material may be obtained in this manner, and that it may be safely done in older animals (heifers or calves some months of age) without impairing their health. It has also been demonstrated that a positive result is much more likely to be obtained in cattle if the epidermis is scraped away instead of being simply punctured or incised.

Animal vaccine material which has been cultivated through many individuals of the bovine species, without passing through the human species at any time, is greatly to be preferred for the inoculation of calves and heifers. If such material alone is used, the possibility of producing a vaccine syphilis in man will be more than sufficiently guarded against. To my mind it seems strange to limit the designation "pure animal vaccine material" or even "animal vaccine material" to those cases in which the virus may be directly traced back to a case of so-called original cow-pox; for what else is this cow-pox but an obscure foundling, picked up in the stall or meadow, and which, in the great majority of cases, is nothing more than a species of variola that has directly or indirectly strayed away from the human family? In my opinion, it is decidedly antiquated to clothe this

disease with "privileges of rank" when it is nothing more than an illustrious offshoot of the parent trunk.

Other sources for the cultivation of other animal vaccine material fortunately have opened up as time went on, and although they are furnished by man himself, they are not to be rejected. Retrovaccinia might be mentioned as the first of these sources; as previously stated, we understand by retrovaccinia, the vaccinia produced in cattle by inoculating them with humanized lymph. Such animal cultures have proved themselves to be equally as specific and safe in their effect upon man as the cultures of the so-called pure animal vaccinia. In time of necessity, moreover, they are easily cultivated from cases of human vaccinia. The contents of the vesicles of retrovaccinia may be employed for the vaccination of individuals of the human species without hesitation, and the practice has frequently rendered the most signal service.

The second of these sources is to be found in the cases of variolo-vaccinia. By variolo-vaccinia (see Variolation of Animals, page 155) we understand those localized pocks resembling vaccinia which are obtained in cattle by the successful inoculation of these animals with human variolous lymph. It has been previously emphasized that it is not allowable to inoculate this variolo-vaccinia back into man from the cultures first obtained, since a return to variola is possible under these conditions, and has already been observed in certain individual cases (Reiter, Chauveau). After the variolous lymph has successively passed through at least 3 or 4 members of the bovine species, and apparently permanently acquired the mild characteristics of the virus of vaccinia, the cultures may be safely employed for prophylactic purposes. It is to be expected in the future that this source of animal vaccine material will also be frequently drawn upon should external conditions make such a course necessary.

Having disposed of the different varieties of vaccine material, we will now consider the hygiene and technique of the act of vaccination. The following rules are to be specially observed:

In all ordinary cases, the first year of human life is without question the most appropriate period for the performance of the first vaccination. It is unreasonable to defer the procedure until a later time, since the danger of infection with human variola is unfortunately but too common in most parts of the world. Such a delay is all the more irrational, since even delicate and weakly children almost always bear the procedure of vaccination without any impairment of their health. Nothing but a permanent and severe illness of the child

throughout this entire period can be designated as an absolute contra-indication, and this is to be no longer considered if smallpox makes its appearance in the neighborhood or in the immediate vicinity. If such is the case, vaccination must be immediately performed in all the non-vaccinated children without exception, and the procedure is not to be delayed too long even in the new-born (imperative vaccination!).

If this imperative indication for vaccination does not exist at the time of birth, the most desirable period within the first year of life will naturally be selected. The period usually chosen is that between the fourth and sixth months. At this age the great majority of children have become sufficiently accustomed to extra-uterine existence to enable them to endure this little operation with its subsequent inconveniences. By performing vaccination at this time, we are not handicapped by the teething of the child, which not rarely causes a lessened resistance to pathogenic influences. It consequently follows that, if no special contraindication exists, the child should be vaccinated before the first troubles of dentition have manifested themselves, or, in other words, before the beginning of the second half of the first year of life.

The further question as to whether every individual, without exception, is to be vaccinated during childhood is to be simply answered by an absolute affirmative, since there are no allowable exceptions to this rule. Special mention should be made of those rather rare cases in which the family history might awaken the suspicion of the existence of hemophilia in the individual to be vaccinated. This possibility is always to be remembered in the children of bleeders, the danger being particularly imminent if the children are of the male gender and if their mothers, though not actual "bleeders" themselves, have hemophilous antecedents (the law of the atavistic heredity of hemophilia). Experience has shown, however, that there is no great danger involved in the vaccination of bleeders, provided that the corium is not injured and a consequent hemorrhage caused by the performance of the operation. Since the introduction of the vaccine material into the deeper layers of the epidermis is amply sufficient for the purpose of vaccination, it is fortunately unnecessary to exclude the children of bleeders from the blessing conferred by the procedure.

The act of vaccination is a most simple one, and yet its proper execution requires care and precision as well as the observance of certain precautions. The outer side of the arm is usually chosen for

the site of the vaccination. For cosmetic reasons, the portion situated immediately below the shoulder is selected, since the scar may subsequently be covered by even a short sleeve. Immediately before the vaccination, this region of both arms is carefully cleansed with moist carbolic or salicylic-cotton, and then washed off with boiled sterile water. The stronger disinfectants, sublimate-cotton particularly, are not to be used for this purpose, since their employment diminishes the chances of obtaining a successful result. The vaccine physician should also thoroughly convince himself that the individual to be vaccinated has had a general bath and that his underclothing is clean. The children of the poor should not be vaccinated in their homes, but in the public vaccine stations, which should always be previously well cleansed and ventilated. It is only by the application of all these precautions, the necessity of which is at once apparent to every physician, that accidental wound infections—an undesirable complication of vaccination—are almost surely excluded and the chances of securing a typical and uncomplicated case of vaccinia are greatly increased.

Vaccination is best performed with a carefully cleansed vaccine lancet, which is not to be previously dried with an ordinary pocket handkerchief, but with salicylic cotton. Two or three shallow scarifications, 2 to 3 centimeters in length and at a distance of about 1.5 centimeters from each other, are made in an oblique direction upon the upper and outer portions of both arms (4 to 6 incisions altogether). The cutting edge of the instrument should not injure the corium, but simply penetrate as deeply as the rete Malpighii of the epidermis. The vaccine material, which has been held in readiness, is now immediately and carefully introduced into these scarifications by means of the same lancet. The vaccinated regions are then left exposed to the air for some minutes to facilitate the drying of the vaccine material, and subsequently covered with a layer of sterile cotton for the next twenty-four hours.

In the early years of vaccination, following the method of Jenner, one puncture or incision (or at most two) was considered to be sufficient, but it later became customary to make a somewhat greater number of scarifications (4 to 8), because this increased number not only made a successful result more likely, but the immunity obtained seemed to be of greater duration (Bohn, L. Pfeiffer, and others). At the present time, scarifications are generally preferred to simple punctures, for similar reasons. If good human lymph or good animal emulsion is employed, it is not necessary to scrape away the epidermis (as is done in the calf), or carry out any of the more painful methods, as the simple scarifications will nearly always suffice. Experiments have shown that if the indi-

vidual is at all susceptible, the vaccine material will be taken up almost immediately (Bosquet).

If in spite of the proper performance of the first vaccination of a child a negative result is obtained, the procedure is to be repeated after some months. In these cases it is well to increase the number of scarifications to 8 or 10 (divided between the two arms), but the remaining details of the operation should be carried out just as before. If the second vaccination should also fail to take, the case is [almost certainly] one of those rare instances of natural immunity. It does not necessarily follow that this immunity will be permanent; the patient is to be subsequently kept under control observation and the vaccination repeated at not too lengthy intervals. As far as the time of their performance is concerned, these repeated vaccinations are subject to the same regulations as those governing revaccination, although the principles in the two conditions cannot be said to be identical. It is of particular importance that they should be performed as often as there is any possibility of exposure to variola.

This natural immunity (whether it be temporary or permanent) against vaccinia forms a corollary to the similarly observed immunity (temporary or permanent) of some individuals against variola. Since variola and vaccinia are only different varieties of the same affection, it is a case of " ἓν διὰ δυοῖν " in both instances. Nothing definite is known as to the cause of this natural immunity against vaccinia and variola. It is possible that a so-called intra-uterine vaccination may be responsible for certain individual cases of this kind. The theory of intra-uterine vaccination is based upon the supposition that a fetus may be infected through the placental circulation by a successful vaccination of the mother during the later months of pregnancy, and that it may thus be rendered immune to the first, or even to the second, vaccination performed after its birth. This sounds very plausible, but positive proofs of the occurrence of this chain of circumstances are nevertheless wanting.

If the effect of the first vaccination is positive and normal, as is usually the case, it is not necessary to materially change the mode of life of the child during the development and disappearance of the vaccinal affection. It is neither necessary nor beneficial to omit the daily bath at this time on account of the vaccinia. Particular care should be taken to prevent the bath-water from coming in contact with the vesicles during the stage of desiccation, since it softens the crust and causes its premature separation. During the acme of the inflammatory process, a marked swelling usually appears at the site of the vaccination. This is rather to be desired, since it aids in the attainment of the protective effect conferred by the procedure. If the sensation of tension is uncomfortable, it may be greatly eased by a local application of vaselin.

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THE NORMAL COURSE AND SYMPTOMS OF HUMAN VACCINIA.

In the great majority of first vaccinations the course of the vaccinia shows a surprising uniformity in the times at which the phenomena of the disease make their appearance. With the exception of entirely accidental occurrences, these phenomena tend to vary in degree, but not in character. It is, therefore, true that the clinical picture of vaccinia is subject to less variation than that of any other pathologic process. The designation of "normal course" for this series of phenomena consequently means nothing more than a simple description of the actual conditions; in this instance, it possesses the significance of a rule that has few, if any, exceptions.

The normal course of human vaccinia may be divided into different stages which correspond to the phases of development of the local eruption. The affection, like other infectious processes, is introduced by a period of incubation. The incubation period of human vaccinia

nearly always lasts three days; it may rarely be shorter (two days), and in still rarer cases it has been of longer duration (four to five days). During this latent period the site of the vaccination shows nothing abnormal, except a temporary inflammatory reaction in the immediate neighborhood of the punctures, which is of no significance, and usually disappears within thirty-six hours. There is nothing to indicate that an infection has taken place; the first evidences of this being the typical appearances which first become manifest at the site of a vaccination at the end of the third day.

These local changes mark the sharp transition from the period of incubation to the stage of development (period of efflorescence or eruption of the disease). At the end of the third or the beginning of the fourth day flat, elevated, intensely red papules of oval or oblong outline are observed, which correspond in position and extent to the previous punctures or scarifications. These papules are firm to the touch, and are soon surrounded by a narrow zone of marked hyperemia (inner halo or inner areola). During the course of the fifth day these papules become surmounted by vesicles, situated centrally at first, but which soon extend to the periphery (usually on the sixth day) and become filled with a clear fluid (vaccine lymph). These structures are known as Jenner's vesicles and strikingly resemble the pocks of true human variola in the peculiar luster of their surfaces (like mother-of-pearl or alabaster), in their central umbilication, and in their multilocular structure.

Complete development is usually attained upon the seventh day; the vesicles of Jenner are tensely filled with clear lymph, which is particularly adapted for use in subsequent vaccinations. In the mean time the previously mentioned zone of marked hyperemia, or areola, has not only become distinctly broader, but is also surrounded by a second area of mild hyperemia, which gradually fades away into the surrounding tissues (outer halo, outer areola). If the vaccine pocks are placed closely together, their individual outer areolæ tend to partly or completely coalesce at this time.

If it is desired to employ the human vaccine lymph for further vaccinations, it is both customary and advisable to leave one or two of Jenner's vesicles intact. This is done in the interest of the individual (child) furnishing the lymph, since it guarantees to him a sufficiently permanent protection.

From the statements of vaccinated adults it has been found that the development of human vaccinia during the stage of eruption is attended by sensations of itching and tension, which become milder

during the stage of full development, but do not entirely disappear. At this time there is a complete absence of the more marked local discomforts, which regularly make their appearance during the following period (suppuration); commencing with the fifth day, however, a slight elevation of the body-temperature, with a corresponding increase in the pulse-rate, is by no means uncommon, though the general condition is otherwise unimpaired. This precursory rise of temperature may be entirely wanting, but when present it is usually characterized by a gradual ascent. The height of this temperature curve bears no relation to the actual vaccine fever, which rarely fails to make its first appearance at the beginning of the second week. This is also the time at which new and significant changes occur in the local vaccine pocks.

The contents of Jenner's vesicles remain fairly clear until the eighth day, when they commence to show a more distinct cloudiness, which marks the beginning of the stage of purulent transformation (suppuration or maturation). The individual vesicles undergo all those characteristic changes which are peculiar to variola, and which have been previously described. They become opaque and distinctly yellow, they lose their peculiar pearl-like luster, and the umbilication almost completely disappears, giving place to a uniform elevation of the surface. All these changes of appearance, due to suppuration, become more completely developed, reaching their acme upon the ninth, or at the latest upon the tenth, day. Unmistakable signs of the stage of involution or desiccation now make their appearance.

From the first appearance of suppuration, however, the changes in the immediate and remote surroundings of the vaccinia are more noticeable than those occurring in the pocks themselves. While the purulent metamorphosis of the vesicles of Jenner is first indicated upon the eighth day, both the inner and outer areolæ, which have previously shown a moderate degree of hyperemia, become intensely congested within a few hours, and to this redness there is added a most marked and acute swelling. The entire vaccination area now forms a single elevated plateau, fiery red in color, firm and resistant to pressure, and bearing the vaccine pocks upon its surface. The edges of the plateau fade away into the surrounding tissues, which are also red and swollen to a considerable extent. In the course of the ninth, or even of the tenth day, it is consequently not uncommon to observe that the remaining portions of the arm are the seat of general redness and distinct tumefaction. At this time the axillary glands are slightly swollen and somewhat sensitive to pressure.

In regular cases of human vaccinia, certain general symptoms are invariably associated with these phenomena which are observed at the height of the local process. The amount of general disturbance shows no inconsiderable variation, and seems to be particularly dependent upon individual idiosyncrasies. Children show more or less distinctly that they are not feeling well by their restless sleep, peevish disposition, and lessened appetite; adults complain of general malaise and of painful sensations not only in the affected arm, but also in other regions of the body. Headache may be present and pain in the back; or lumbosacral pain is still more frequently observed. Giddiness, sleepiness, nausea, and sometimes even vomiting may be present. All these symptoms of an apparently toxemic disturbance of the general system are fortunately not of long duration in vaccinia, and they rarely attain a violent character; they nevertheless betray their real nature by the fact that they are regularly accompanied by fever.

The fever of vaccination, sometimes present to a mild degree toward the end of the period of development, always manifests itself with the beginning of suppuration upon the eighth day, and usually extends well into the tenth. The height of the fever is variable, though evening elevations to 39° C. (102.2° F.) and over are by no means rare. The temperature almost always falls rapidly before distinct evidences of desiccation are visible in the exanthem, and if no complications are present, the fever does not return. With the fall of temperature, all the previously mentioned symptoms of general disturbance of the system quickly and permanently disappear.

The retrogression of the local symptoms commences at the end of the tenth or at the beginning of the eleventh day, and, as far as the involution of the vaccinia is concerned, the process is always slow and gradual. The inflammatory congestion, which preceded the suppuration of the vesicles of Jenner, disappears much more rapidly, the hyperemia of the adjoining area having completely vanished by the tenth day. At the same time a sinking-in of the previously mentioned vaccination plateau is also noticed, together with a diminution of resistance and tenderness to the touch. During the following days this elevation completely disappears, as the pocks gradually dry up. The epidermis undergoes some desquamation and there is left a brownish discoloration of the skin which remains for a certain length of time.

The drying-up of the vaccine pocks and the separation of the vaccination scab (desiccation and decrustation) usually comprise a

period of from ten to fourteen days. The process exactly resembles the similar stage of variola, the changes simply being localized to the vaccination area. Since a fully developed first vaccinia causes deep-seated alterations in the skin, the clinical course and the pathologic anatomy of the lesion resemble the completely developed individual pocks of a severe case of variola vera discreta more than they do the so-called varioloid pocks. The periods of desiccation and decrustation in these two diseases are consequently of longer duration, and in severe cases of variola are always followed by the formation of pits or scars. In the case of vaccinia, however, these scars are always left behind, but they are localized to the site of the vaccination. The most important changes taking place during these periods are worthy of a brief consideration. At the beginning of desiccation the pocks are usually of a honey-yellow color, but this soon gives way to a dirty brown, and at the time of decrustation the lesions are almost black. During this time the pustule itself shrinks up into a hard, brittle, irregular scab, which is traversed by numerous fissures. This scab remains firmly adherent to the underlying structures for quite a number of days, and seems to sink more and more deeply into the cutis. The scab usually separates from the periphery toward the center. If it is cast off spontaneously, and not torn off prematurely by accident, the fresh vaccination scar is seen to be fully formed. The scar is deep and its dimensions approximately correspond to those of the preceding pustule. It is therefore somewhat elongated at the present time, since vaccination is now usually performed by means of scarifications instead of by small punctures. The fresh vaccination scars, like the cicatrices of variola, have a rosy appearance at first, which is due to their vascularization, but they subsequently become smaller and white in color from the contraction of the newly formed connective tissue.

This description has included all the chief points of the entire course of normal human vaccinia. Of the accidental symptoms that may also be observed, brief mention will be made of two, since they do not really come under the subsequent heading of Anomalies and Complications of Vaccinia. Both of these accidental symptoms occur during the suppurative and febrile periods.

1. On the eighth or ninth day a macular erythema sometimes spreads rapidly over the entire body of the vaccinated individual, which, from its transitory nature and other characteristics, absolutely resembles the roseola variolosa (an initial erythema somewhat like measles) of a beginning human variola. It is scarcely necessary to

emphasize the fact, that this is an additional piece of evidence for the identity of vaccinia and variola.

2. In addition to the fully developed vesicles of Jenner, a moderate number of so-called accidental or accessory pocks are occasionally seen in the neighborhood of the vaccination site. These pocks usually run an abortive course, and very often do not progress beyond the papular stage. It is fair to suppose that they sometimes owe their origin to the previous existence of small excoriations, into which some of the vaccine material has been subsequently introduced by the clothing. They are more frequently, however, an expression of the passage of the vaccine virus into the lymphatics, since they tend to make their first appearance at that period of the course of vaccination in which there is a reproduction of the virus in the chief vaccine vesicles. The abortive course of the great majority of these accessory pocks is also best explained by this latter supposition, since the protection acquired by the vaccinated individual is almost perfect at this time.

If we again review the individual details of the clinical course of human vaccinia, we are most forcibly impressed by the fact that this affection, in its most essential nature, can be nothing else than an inoculated variola produced by a mitigated and fixed virus, and that the general eruption and its concomitant symptoms are all that are wanting to complete the picture. This conception becomes still more plausible when we consider that some cases of inoculated variola run their course without any general eruption, and that these abortive cases confer upon the inoculated individual just as complete an immunity as do the others. It would be following out the same line of reasoning to conclude that the protection afforded against variola by vaccinia probably exists only because both affections are essentially of the same nature and simply differ from each other in their intensity.

THE PROTECTIVE EFFECT OF VACCINATION.

The establishment of an immunity against variola is not only the aim, but also the regular effect, of every successful vaccination in non-vaccinated individuals or in those who have not had smallpox. The immunity so obtained is generally a temporary one for the individual, and not permanent, as was originally believed. It is nevertheless true that in all cases the immunity is absolute for a certain variable period of time. This statement cannot be doubted, for

many thousands of experiments have shown that an attempted variolation is always without result when performed upon an individual who had quite recently been vaccinated.

Although intentional vaccination had been performed before the time of Jenner, as had also the intentional attempted variolation of individuals who had been accidentally infected with vaccinia, Jenner was the first to thoroughly demonstrate by experiments the fruitlessness of variolation in quite a number of persons whom he had previously vaccinated. Immediately after the appearance of Jenner's first publication, his double experiment was repeated, and his findings were confirmed both in England and upon the Continent. B. Pearson alone (1800–1803) carried out such experiments in no less than 5000 individuals, and other noted medical vaccinators at that time also endeavored to furnish a great quantity of statistical material from their own experience and practice for the positive decision of this elementary question. While these experiments are no longer necessary, they are occasionally carried out for the purpose of demonstration. B. Huguenin, for example, in 1879, performed Jenner's double experiment upon his own person.

The first successful vaccination of individuals who have neither had smallpox nor been vaccinated confers upon them the same temporary immunity against vaccinia as it does against variola. If an individual is revaccinated a short time after a successful vaccination, the result obtained is always a negative one. A similar result also follows the vaccination of individuals who have passed through an attack of variola, provided too long a time has not intervened. These negative results have received ample confirmation, and constitute extremely valuable corollaries to the failure of variolation after a successful vaccination. They prove that the conditions upon which the immunity of the individual depends are the same in variola and vaccinia, or at least that they show no marked deviation. If this is firmly established empirically, it may also be supposed that the appearance, the duration, and the disappearance of the immunity against vaccination show no real difference as regards variola or vaccinia. As a matter of fact, it might finally be added that there is not a single clinical experience that speaks directly and unequivocally against this supposition.

One faulty objection that has been made against this supposition is that a successful vaccination has been performed upon individuals who had been in intimate association with smallpox patients and yet had not been infected with variola in the natural way. Since these cases were usually instances of successful revaccination, it has been claimed that such positive results show that the protection against vaccinia is lost before that against variola. This conclusion is not justifiable, however, since it has been rightly emphasized by Th. Lotz that inoculated vaccinia

and variola acquired accidentally (from simple association) have not the same pathogenesis. Simple association with smallpox patients does not by any means surely guarantee the actual introduction of the smallpox contagium, and consequently does not necessarily cause the disease in individuals susceptible to variola. The actual introduction of the vaccine virus, however, is quite another matter, since this always produces vaccinia in the individual if he is at all susceptible to the disease. It is clear that the only way to decide the question as to whether an individual is susceptible to a virus is by inoculating him with that virus. This practically means that those individuals who are susceptible to the introduction of vaccine material would also be susceptible to variolation, if this procedure were carried out instead of vaccination.

For the production of a temporary protection against variola and vaccinia by a single vaccination it is necessary that the result shall be completely successful. It is consequently requisite that the procedure should be followed by a three-day period of latency, that the development of the vesicles of Jenner in the vaccinated individual should be typical, that the inflammatory vaccination plateau should regularly appear as previously described, and, finally, that a sufficient scar should be left as a visible result of the process. A certain protective effect, for a more or less lengthy period of time, can be expected only when all these requirements have been fulfilled. The negative result of a single vaccination, on the contrary, guarantees nothing, and a second vaccination is urgently indicated within a short period of time. If the second vaccination is likewise without result, past experience shows that it is highly probable that a temporary natural immunity against both vaccinia and variola is present. Clinical observation also shows the urgent necessity of watching over such an individual and vaccinating him from time to time, since this temporary security by no means excludes every future danger of infection. The positive or negative results of such later vaccinations alone will definitely decide the question whether the individual was immune at that particular time. The rudimentary result of a first vaccination and a vaccinia which pursues a markedly atypical course both require a subsequent control vaccination. If the individual proves completely refractory to this second vaccination, we may conclude that the first vaccination, in spite of its rudimentary and clinically abnormal character, sufficed to completely eradicate for a time the existing susceptibility to vaccinia and to variola. If the second vaccination runs a regular course, it is to be supposed that there was some technical error in the performance of the first procedure. These facts will suffice to determine the significance and subsequent value of a positive result.

We must differentiate this subsequent immunity from the im-

munity that occurs during the course of a successful vaccination. This point is not devoid of clinical interest, since the important question of the time of the appearance of the protective effect hinges upon it. It is self-evident that the protection cannot be perfect at the moment of the vaccination; upon the other hand, experience has repeatedly proved that the protective effect is complete by the time the vaccinia has run its course. The question that remains is as to the stage of the vaccinia in which the vaccinated individual becomes immune. Observation and experiment have taught the following facts.

During epidemics of smallpox it has been observed that vaccinated individuals not rarely become infected with variola during the course of their vaccinia. Such experiences teach that double infections are possible and that inoculated vaccinia and naturally acquired variola may occur together under certain circumstances. In such cases the outbreak of the initial symptoms of variola is far more frequent in the first week of the vaccinia; they commence more rarely in the middle or at the end of the second week, and have scarcely ever been observed in the course of the third week. If these empiric facts are considered, together with the observation that the usual duration of the period of incubation of a naturally acquired variola is from ten to thirteen days, it naturally follows that in such cases the variola has an opportunity to completely develop by the time that the immunity should be conferred, and usually overcomes the protective effect of the vaccination. The great majority of these outbreaks of variola during the course of vaccinia without doubt depend upon a preceding variolous infection, the date of which may have been long before that of the vaccination, but which may always be at least approximately computed. Clinical experience further shows that the intensity of the arising variola bears an inverse ratio to the period of the vaccinia in which it develops. The earlier the variola appears, the less the time left for the vaccinia to develop its own pocks, the more severe will be the course of the variola; and if the smallpox breaks out very early after the vaccination has occurred, the vaccine pocks may be stunted in their development. If the variola first becomes manifest at about the middle of the first week, the eruption of the variolous exanthem corresponds in time to that of the vaccine pocks, and in such cases there are observed florid variolous pocks and suppurating vaccinia pustules side by side at the beginning of the third week. Finally, if the invasion of variola does not occur until the end of the first week or later, the moderating influence of the

advanced vaccinia is very distinctly perceptible, and the variola is very mild or even rudimentary in character. Of course, there are exceptions to these general rules, and the individual peculiarities of every case cannot always be explained, but these exceptions are not frequent enough to invalidate the rule. The ordinary course of events clearly shows that coincident variola and vaccinia are antagonistic to each other, and that the affection which takes hold of the individual first dominates the subsequent chain of symptoms.

Since variola has been observed to develop during the course of vaccinia and apparently coexist with it harmoniously, certain authorities, Curschmann especially, would conclude that the two diseases are specifically different from each other. In my opinion these cases offer no unequivocal argument in favor of this supposition, and there are many weighty objections against it. These occurrences can all be explained by the fact that the specific protection of vaccinia against variola (a disease of the same species) has not sufficiently matured at that particular time. The results of both infections then balance each other, and they both develop apparently independently of each other. If this particular balance does not exist, the antagonism between the two diseases, which is an important argument for their homogeneousness, almost always becomes unmistakably noticeable.

In reference to the production of the protective effect, the clinical observations and experiences previously quoted show that this protection cannot be developed at any one particular time in the course of a vaccinia, but that it is the result of a gradual accumulation of a number of individual influences. When the vaccinia enters upon the stage of suppuration (beginning of the second week), this accumulation seems to have so far advanced that the variolous infection is but rarely able to cause any considerable pathogenic effect.

Entirely similar conclusions have also been reached in an experimental way. When variolation is performed at the commencement of the course of inoculated vaccinia, with the exception of the localized variola pustules, nothing is obtained but quite a rudimentary general exanthem, which begins in the period of suppuration of the vaccinia (Sacco). If the variolation is performed somewhat later, nothing is produced but local and abortive pocks; and if it is carried out at a still later date, no result whatever is obtained. Inoculated vaccinia has been employed far more frequently than inoculated variola, however, for the purpose of determining at what time a positive result failed to appear after a revaccination (Zöhrer, Kühn, and others). Such experiments showed that after the sixth day every further vaccination was absolutely without effect; revaccinations upon the preceding days, on the contrary, in general gave positive results.

A marked difference was noted, according as the second vaccination was made earlier or later within the period of time indicated. While the very early second vaccination usually shortened its own latent period and showed an effort to completely catch up with the primary vaccination toward the end of the week, the second vaccinations, made later, did not proceed so far, and were arrested or aborted in their course. These experiments likewise indicate, in a most striking manner, the gradual development of a vaccinal protection; at the same time they also teach that this protection is practically always complete by the beginning of the second week.

These facts, obtained by observation and experiment, together harmoniously furnish a most urgent indication for the practical prophylaxis of smallpox. They demonstrate the necessity of at once performing vaccination if the possibility of an infection with variola is present and show the folly of waiting until the actual outbreak of the disease. Since inoculated vaccinia has a much shorter period of incubation than naturally acquired variola, every day gained by the early introduction of the vaccine material is of inestimable value to the threatened individual. If variola subsequently develops, the chance of obtaining a mild attack of the disease is much greater than if the individual is left without any protection. If a vaccination is made early enough in the period of incubation of the variola, however, it is beyond question that the disease may not seldom be completely aborted.

The important theoretic question as to what actual biologic processes in the body of the vaccinated individual are responsible for the production of the protection remains, as yet, unsolved. Earnest endeavors to answer this question have, indeed, not been wanting (Pohl-Pincus, Wolfberg, Ackermann-Wolf, L. Pfeiffer, and others). But it would be claiming too much to declare that any of the existing hypotheses are sufficient. In my opinion, however, it is entirely wrong to apply to the explanation of the protection afforded by vaccination the modern experiences as to the rather obscure origin of antitoxins in the blood-serum of animals immunized against diphtheria and tetanus. These processes cannot be compared clinically, since every one knows that such immunity is only of a very temporary nature. In the production of vaccinal protection, on the contrary, there is, as a rule, a change of constitution which persists for years, and which could hardly have as its sole cause any chemical peculiarity of so perishable and changeable a tissue as the blood-serum. Since a sufficient and completely satisfactory theory of

vaccinal protection is wanting, it seems to me that any further con-
sideration of this subject is so confusing that it would be out of place
in this article. There is still another. point, however, which is deserv-
ing of a brief explanation. The duration of the vaccinal protection
and the manner of its disappearance are certainly a most important
part of the practical side of vaccination. This question must be
considered for the purpose of determining when precautions should
be taken to renew the protection which has become deficient. The
answer is unfortunately a complicated one, since there is evidence to
show that the duration of absolute immunity after a single vaccina-
tion extends over no definite period of time, but that it is subject to
great individual variations. After a single successful vaccination in
childhood it has sometimes been observed that all subsequent attempts
at vaccination failed, and that the individual never acquired variola
in spite of frequent exposure to the danger of infection. In these
cases it is certainly justifiable to assume that the single vaccination
has caused a permanent protection, just as one attack of variola
usually renders the individual immune to any subsequent invasion
of the disease. What is the rule for variola, however, is unfortunately
only the exception for a single vaccination. It much more frequently
happens that the individual reveals a fresh susceptibility, at least
to inoculated vaccinia, after a more or less lengthy period of time.
Cases are sometimes encountered in which a revaccination is successful
after the short span of two or three years, but such occurrences are
even still more exceptional than the instances of a permanent protec-
tion. They are consequently no guides for either practical purposes or
legislative action, and this is especially true, since the corollary of a
similarly early attack of variola after vaccinia is as yet wanting.
The renewed susceptibility to inoculated vaccinia, nevertheless,
always makes one fearful lest an infection with smallpox would have
been possible in these cases if the variolous virus had found an oppor-
tunity to effect an entrance into the system. If a longer period of
time has elapsed since the vaccination, a secure protection against
variola is to be no longer counted upon; the epidemics of smallpox in
the nineteenth century sufficiently demonstrated that the number
of cases in individuals vaccinated but once was far from infrequent.
The individuals who were vaccinated in the first year of life were
scarcely ever attacked until after the fifth year, and it was not until
the tenth year was reached that the number of individuals attacked
rapidly increased. It might be stated from these observations that
the average duration of the protective effect of a single vaccination

is about ten years, and that it certainly does not extend much beyond this period. The vaccination statistics confirm this view to a certain extent, since they show that after the tenth year about 60% (and over) of all individuals vaccinated in early childhood show a re- newed susceptibility to inoculated vaccinia which is more or less pronounced.

The duration of a vaccinal protection seems to be in some measure dependent upon the number of scarifications and vaccine vesicles. This number has nothing whatever to do with the immunity of the individual for the time being, for Jenner and his first fellow-workers were always satisfied with one, or at most two punctures and vesicles, and nevertheless rendered the vaccinated individual secure against direct variolation. As Jenner's dogma of the permanency of a vac- cinal protection gradually sank into its grave, it was proposed to increase the effect of the vaccination upon the system by making an increased number of punctures, and in this manner to attempt to render the protection more permanent (Robert, Versen, Marson, and others). This new custom proved better than the old one, and has been generally adopted, so that at the present time 6 or 8 well- developed vaccine vesicles at the first vaccination are supposed to guarantee an approximate vaccinal protection of about ten years. Experience sanctioned this custom, since it was noted during small- pox epidemics that those individuals who had been once vaccinated, but who bore no distinct scar, or only one or two, were attacked and killed by the disease in great numbers (Oppert and others).

Bohn also states that the few cases of mild variola coming under his observation in vaccinated children between five and ten years of age almost always occurred in those who possessed but one typical vaccina- tion scar, and that he was usually able to successfully revaccinate children with such scars after five years. It might also be mentioned as a historic reminiscence, that the old Bavarian vaccination law required a revaccina- tion of all these children likewise within five years. In view of the fact that the number of cases of variola shows a striking increase after the tenth year in individuals who have been vaccinated in early childhood, the present vaccination law of the German empire declares the twelfth year to be the legitimate time for the compulsory revaccination.

In the great majority of cases the disappearance of the immunity seems to be a gradual and not a sudden process; it occurs in such a manner that the full susceptibility to variola does not immediately manifest itself. The actual proof of this is to be found in the fact that the great majority of cases of variola occurring between the tenth and fifteenth years of individuals vaccinated in early childhood still

cling firmly to the clinical type of so-called varioloid, and that the severe cases (variola vera) do not show any marked increase in number until after puberty. History furnishes us with an entirely analogous fact, since the variolous nature of these mild affections of vaccinated individuals was obstinately contradicted, until toward the end of the third decade of the nineteenth century, when the increasing malignancy of these so-called varioloids gradually led to a proper conception of the true state of affairs. Some years, however, passed before the correct idea was really acquired, and these should naturally be rather subtracted than added to the period in question. We thus learn two things from these historic data: first, that the vaccinal protection does not usually completely disappear at once, but that it gradually fades away; and, secondly, that in a great proportion of all individuals who have been vaccinated but once little or nothing is left of this originally absolute protection after a period of about twenty years.

Revaccination is consequently a most urgent necessity. It is to be carried out in early life if possible, and also subsequently repeated at appropriate times. The great value of revaccinations consists in the fact that, if performed at the proper time and at certain intervals, they are actually able to do what a single vaccination fails to accomplish. The manner in which the question of revaccination has grown and the prevalent opinion upon the subject will be briefly indicated in the following section.

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REVACCINATION.

THE idea of renewing the worn-out immunity against variola by repeated vaccination at definite intervals could arise only after the belief in the perpetual effectiveness of the primary vaccination was controverted. This change in belief manifested itself first in the second decade of the nineteenth century, though almost a further ten years was required before revaccination as a prophylactic measure was actually put into practice. This long period of incubation between the theory and the practice is less surprising when we realize that the majority of cases that were attacked by smallpox subsequent to vaccination occurred not at once, but gradually, and were therefore less strikng; and, further, when we take into account that it was exactly the inaugurators of vaccination, with Jenner at their head, who insisted most obstinately on the perpetuity of the protection afforded by vaccination. Without much exaggeration, it may be affirmed that the most zealous advocates for vaccination proved the greatest obstacles in the way of revaccination, though they came round with the development in time of the idea. Finally, another circumstance, mentioned before, added to the confusion of the true conditions, to the protraction of the discussion, and indirectly to the delay in the advance of prophylaxis—namely, it became questionable whether or not the many slight cases of variola in the vaccinated should be considered as true smallpox. "If varioloid had nosologic-ally little or nothing to do with true smallpox, how could repeated vaccination act prophylactically against it?" said the opponents of revaccination.

It was only after this uncertainty had been settled by Thomson that the doctrine as to the permanent preventive effect of vaccination was finally exploded. Varioloid was now stamped as a mild or modified form of variola. By this avowal, though it was not the absolute truth in every case, at least this much was acknowledged, that the protection accorded by vaccination lasted only a certain time, and that the susceptibility to variola very frequently recurred, even if only to a lesser degree. Moreover, it was again forcibly urged, as had been done throughout two entire decades, that even an attack of variola itself did not always succeed in making a person absolutely immune for the rest of his life, and this eventually did

away with the doubtful opinion that the milder and much less active vaccinia could be more lastingly effective than variola in highly predisposed subjects. It was now no great step from this acknowledgment to trials of revaccination, for it became self-evident that revaccination was a practical, as well as a theoretic, requirement. In regard to this, it was first necessary to try if, after the lapse of a considerable time, vaccination would take again on the same subject, which would determine, not only a renewed susceptibility to vaccine, but also a renewed eradication of the susceptibility to variola.

The question stood thus at the beginning of the third decade after Jenner's publications. The conspicuous merit of priority at this time both as regards preliminary investigations and in the matter of revaccinations on a very large scale belongs especially to the German physicians Wolfers and Dornbluth, and further to Harder in St. Petersburg; though at about the same time Lüders and Hufeland were demonstrating from *à priori* grounds the necessity for revaccination. The revaccination movement had its beginning in the year 1824, and received decided impetus from the severe epidemics of smallpox that raged over the greater part of Europe during the subsequent years up to 1833. The immediate results in individual cases from the numerous revaccination experiments surprised the investigators, yet on the whole they proved that the theory of revaccination was correct. In not a few cases there appeared, after the reinoculation of cow-pox, typical Jenner's vesicles, by which it was made clear that these persons had recovered complete susceptibility to cow-pox, and presumably also to variola. In some the revaccination failed entirely, which proved that in these the primary inoculation still protected against cow-pox, and therefore also against variola. Finally, it was learned for the first time, from a very large number of cases, that there was an undeveloped form of vaccinia, which was afterward called vaccinoid, or modified vaccinia (Harder). Though at the beginning, and for a short time afterward, there was some perplexity as to the meaning of this peculiar product of revaccination, it was later considered to be, and very appropriately designated, a vaccinal analogue of varioloid (or modified smallpox), and this significant name remained applied to it. It was consequently placed parallel to the varioloid attacks in vaccinated subjects, whose thanks for their mild attack were due to the previous vaccination. Moreover, it was naturally concluded in these cases that the modified results of the revaccination were the effects of a reawakened, though not yet marked, susceptibility to vaccinia and variola.

These conclusions created a certain clearness in the theoretic consideration of the subject, and they were not without favorable influence on the practical management of revaccination. Within a short time revaccination claimed many zealous and active partizans, who made it their duty to put forward repeated proofs of greater or less significance. Added to this, time showed the effect of revaccination in the prophylaxis of variola; for in the next epidemic of smallpox which proved to be malignant, the marked immunity of the successfully revaccinated was striking, especially in contrast with the slight resistance manifested by those who were vaccinated only a long time before, or those who were never vaccinated. The same experience has been confirmed in every epidemic up to the present so plainly that, to the unprejudiced, there remains no doubt as to the usefulness, nay, even the necessity, of revaccination.

In the mean time these early favorable effects of revaccination were paving the way in different countries for a State recognition of its necessity, which is to be highly recommended. Every one of the States of the German Confederation at that time (except Austria), in quick succession, made revaccination compulsory in the army, and showed thereby a foresight as to its importance and usefulness, on which they are to be congratulated.

Würtemberg made the laudable beginning, and in 1829 gave orders, and 4 years later (1833) passed a law, by which all recruits, without exception, must be revaccinated. Prussia followed only one year later with a similar law (1834), then Hanover (1837), Baden (1840), Bavaria (1844), and in succession the other smaller States; consequently, at the middle of the nineteenth century, with the already mentioned exception of Austria, all the German troops were in possession of revaccination, and they were, even then, reaping the evident fruits of this foresight. Finally, how thoroughly the benefit of a thorough revaccination was proved in the German army, in contrast to the pitiable condition in the French army during the great German-French war, has been already mentioned, and must remain indelible in the annals of history.

Of the other civilized nations, only a few followed the example of Germany, as Sweden (as early as 1849), Austria (as late as 1886), etc. In England vaccination (or revaccination) has been regularly practised for a long time in the navy, but not in the army, while in France and Russia it is compulsory in the army, but the navy is exempt.

In regard to the civilian population, it is only in the German

empire that a decided step for revaccination has been taken by the law of 1874 (see p. 184), though it is truly high time that the question be seriously considered elsewhere, for "Summa semper vis inertiæ."

The most judicious time for the first revaccination is not the twentieth year (or the period of entrance on military service), but considerably before it. According to the conclusions of the previous section, the prophylactic effect of the primary vaccination lasts, on an average, not much more than ten years, and then there arises for the majority of people, a certain degree of susceptibility to vaccinia and variola. Therefore the first revaccination should take place, as is commanded by law in the German empire, in the beginning of the second ten years of life, and not later. The only exceptions, further, that should be allowed to this rule are in the case of those who have passed through a natural attack of smallpox, and are therefore presumed to be permanently immune.

The technique of revaccination is exactly similar in all important points to that of vaccination, both in regard to the vaccine matter and the choice of inoculation site, as well as in the performance of the operation itself. Though, as a rule, in revaccination the number of cross-scratches is somewhat higher than in primary vaccination, this practice is based on the experience that the results of revaccination are much more uncertain than those of vaccination. Added to this there is the conscious endeavor to increase the duration of the effect, and leave to the individual a rich dowry of immunity that may last through life.

The results of vaccination assume in the revaccinated a very much more varied character—that is to say, they differ minutely from those of the primary vaccination. While the result of the latter is usually complete and shows a typical picture (see under "Vaccination"), in the revaccinated it is necessary to distinguish between negative, complete, and modified results, since the degree of susceptibility for the repeatedly inoculated vaccine virus may vary in individual cases within the widest limits. As to the negative result there is nothing, or at most only this much, to say, that after a short traumatic reaction at the site of inoculation, which disappears after one or two days, there is no other local or constitutional disturbance. The complete effect of a revaccination is evidenced by a typical vaccine eruption at the site of inoculation, in the midst of which the Jenner vesicles develop at their proper time, mature, suppurate, dry up, cicatrize— in a word, go through all the earlier described stages of development and regeneration. A difference from the normal course of a primary

vaccination is particularly to be noticed in the severe way in which the inflammatory reaction frequently affects the vicinity of the site of inoculation during suppuration, and further in the general symptoms being frequently well marked. Yet this latter is not ordinarily the rule; on the contrary, a successful revaccination more commonly runs a mild course.

The not infrequent modified results that constitute at least the principal feature in revaccination require a special discussion.

We have already indicated (see p. 214) in a cursory way that these results consist in the milder and frequently rudimentary character of the eruption. In individual cases every degree of variation in duration and severity of the local process may be observed; yet there are besides temporary deviations from the course, which accord with the usual intensity and duration of the specific reaction. The more incomplete the later vaccinoid course, the earlier does the specific reaction usually follow the traumatic one in such a way that the stage of incubation is correspondingly shortened. This frequently goes so far as to cause the commencement of the specific reaction to fall in the course of the traumatic reaction, so that an interval of acute latency does not take place. The actual beginning of the vaccinoid disease is then recognized by the sudden occurrence of itching, at the site of inoculation, which seems to regularly introduce the active process, and immediately afterward by the appearance of hard red swellings. These never develop in those very mild and almost rudimentary cases of vaccinoid into typical papules (with sharply defined margins), but ordinarily disappear after a short existence of about two or three days. If, on the contrary, there appears between the end of the traumatic and the beginning of the specific reaction an interval of latency, even though this is short, we usually see more or less typical papules, and distributed on their surface (especially at the margins), very small vesicles. Yet these rudimentary vesicles quickly dry up, and are soon thrown off in the form of very small yellowish crusts, while the papules themselves remain somewhat longer and then disappear. In a severer grade of modified vaccinia (or vaccinoid) the initial period of latency, after the traumatic reaction, is somewhat longer, the papule formation somewhat more pronounced, and the tendency to the development of vesicles more evident. There arises at the margins of the papules a pearl border of small vesicles about the size of the head of a pin, which take on a herpes-like appearance, and visibly display an inclination to partial confluence. Moreover,

evident signs of an areola interna and traces of an areola externa appear even in these cases where the period of maturity of the vesicles is short, and point to a mild inflammatory reaction in the immediate surroundings and in the tissues somewhat further away, due to the spread of the virus. Yet this is only transitory, and the retrogression and drying-up of the vesicles begin at a time when typical Jenner vesicles would have by no means reached the acme of their development. Further, while these would later show a period of suppuration, with all its severe symptoms, the former show not the least sign of suppuration, or of that inflammatory congestion which is so characteristic in suppurating normal vaccinia papules. Finally, these vaccinoid cases which show the fully developed Jenner vesicle (even to its suppuration) are strikingly differentiated by their more precipitate course, by the incomplete purulent change of the vesicular contents, and especially by the absence of marked congestive symptoms (intense redness and swelling of the skin, intense pain on pressure, etc.); and the same is true, as is self-evident, the more rapid the involution of all the progressive changes.

Vaccinoid (or modified revaccinia) leaves behind no scar, or at most one that is not evident. Moreover, in the latter case it lacks usually those peculiar characteristics common to normal vaccinia scars.

General symptoms (fever, malaise, etc.) are wanting in modified revaccinia cases, or at most are very slight. Yet, as might be supposed, there are occasional exceptions in which, toward the end of the first week, in spite of the slight local reaction, there appears a transitory indisposition, with a feeling of general depression, headache and backache, rise of temperature, and similar toxic symptoms.

The advantage (or utility) of a correctly made revaccination is primarily diagnostic; for according as the result is negative, modified, or complete, it shows sufficiently clearly whether, and in what degree, the individual was susceptible to vaccinia and variola. In regard to vaccinia, the conclusion is absolute and evident, but the further signification in regard to accidentally acquired variola (which is by far the most important) is obtained only by the aid of the premises, the granting of which has been fully discussed in a previous section (see p. 206). Since no single clinical fact stands absolutely against the correctness of these premises, it is unquestionably allowable to consider them correct, and consequently the further conclusion just mentioned in all its fulness as also correct.

The other advantage of revaccination is as a prophylactic measure;

for it has been absolutely determined by a very large number of experiments that a revaccination, when it is successful, and therefore shows normal Jenner vesicles, again brings about complete immunity against any subsequent inoculation (with vaccine) in a manner exactly similar to a successful vaccination. It has been determined, besides, that a successfully revaccinated person may, for example, nurse, or live in the presence of, smallpox patients without serious danger of becoming infected. Finally, the same is true of the conscious or unconscious employment of effects used by smallpox patients (as clothes, bedding, etc.).

A very remarkable case of this last kind, which he knew to be true, was reported to me some time ago by von Ziemssen in a conversation: A soldier of a Pomeranian regiment, who shortly before had been revaccinated with complete success, received permission for a short visit to Greifswald, in order to be present at the funeral of his father, who had died of malignant smallpox. Having arrived at home late and tired, he threw himself regardless of consequences on the bed in which his father had lain and died, and slept throughout the whole night the sleep of the just defender of his fatherland, without any subsequent symptoms.

A revaccination with negative result has no absolute prophylactic value, but only the above-mentioned diagnostic one—namely, that the person in question possesses at the time no susceptibility for either virus (vaccinia or variola). In order to be absolutely certain, a subsequent inoculation may be done. Such persons, according to our experience, may also come in contact with smallpox patients without fear of danger. The rare apparent exceptions to this rule are explained on closer investigation of the patient's history by finding that the infection with variola had already taken place before the (then unsuccessful) revaccination was done.

As to the prophylactic value of modified results, the views of physicians differ. Some wish to ascribe to them no protective value; others, with undoubted right, maintain the opposite opinion. The fact is that persons who show only modified results also show an immunity to infection, even when they come in close contact with variola, and, further, that subsequent inoculation is negative.

In 1865, in the medical clinic at Tübingen (under the direction of F. von Niemeyer), I myself have after four weeks reinoculated about 30 people (most of them medical students, though some also were clinical patients) who had shown modified results after a revaccination. The reinoculation proved negative in all, without exception, and especially in those who manifested at most a very incomplete and rudimentary revaccination.

There is therefore no doubt as to the immediate protective value of the modified, as well as of the complete, revaccinia; and also none as to the importance and utility of the general principle of revaccination. If done at the right time, the revaccination again produces complete immunity, in case this was weakening or was entirely worn out. Moreover, the result of revaccination, according to its degree, demonstrates at the same time in how far it was desirable that the vaccinia protection should be restored to the individual at the time.

The re-establishment of immunity after revaccination is explained in an exactly similar way to the analogous process after vaccination, by the addition (or integration) of the smallest immunizing effects which, in consequence of certain biologic processes, gradually and successively come into existence and accumulate during the progressive development of the revaccinia to its acme (see p. 208). As to the nature of such biologic processes, we can only say that nothing exact is known so far about the reciprocal effect between the living vaccine virus and the living organic cells of the person vaccinated (compare p. 209).

Finally, it is important to consider briefly the durability of the immunity obtained by revaccination. After our experience in vaccination, it was scarcely to be expected that the new immunity acquired by revaccination would in all cases persist through life. And this presumption was verified forasmuch as variola has occurred, after some interval, in successfully revaccinated cases. But the number of cases occurring in revaccinated individuals is inconsiderable, and only in rare instances does such a late attack of variola terminate fatally or even run a severe course. The mere fact, however, proves beyond dispute that immunity produced by revaccination, like that derived from primary vaccination, may in time fail to guard the organism against accidental infection by variola. On the other hand, it is a matter of much more frequent observation that repeated vaccinations, in individuals who have already been revaccinated, continue to "take" and give a positive (modified or complete) result, not only once, but, it may be, several times. Such a positive result is to be regarded as an even more sensitive reaction to renewed disposition on the part of the individual than the contracting of variola, and proves that in a large number of cases the prophylactic power of revaccination is of only short duration.

In not a few cases, on the other hand, revaccination confers lifelong immunity. This is shown not only by the fact that comparatively few individuals, even if they have only had the benefit of one

successful revaccination, are later attacked by smallpox (see above), but also by the more significant observation that in a very considerable number of persons all attempts at revaccination fail, with the exception of the first, which usually yields a positive (modified or complete) result. In these cases it would seem that what traces of predisposition remain after primary vaccination are destroyed root and branch, never to return, by a single successful revaccination. This need not cause surprise if it is remembered that a certain proportion of primary vaccinations in themselves suffice to confer the gift of permanent immunity, all subsequent attempts at revaccination, including the first, remaining unsuccessful.

Whether the number of those who become permanently immune by one revaccination is greater than those who become so after vaccination alone, cannot be absolutely determined, since statistics in regard to this are wanting. Yet this seems to be the case, for otherwise the number of smallpox patients among those who were once revaccinated would be greater than it is, because this figure is far behind the number of smallpox cases among persons who were vaccinated but once (compare the following section).

In the requirements of practice the possibility that one revaccination may be under certain circumstances sufficient to produce an apparently lasting immunity possesses no *à priori* value, and should not be given it. Never beforehand, but only after a revaccination by means of its variable results, can it be determined whether the revaccination was necessary at that moment or not. In practice, therefore, there is no other way or means of intelligent prophylaxis than by the repetition of revaccination at definite and not too long intervals.

This is, then, the well-considered and rational method of treatment of those who have pursued the study of the protective value of vaccination, neither rashly nor indifferently, but with common sense. There still remains, however, one question to be answered, which is both practical and important—namely, what time interval should be allowed between revaccinations, after the first successful one? In reference to this, the following may be said:

Since the primary vaccination, when done in infancy with its usual complete success, is generally reckoned to be a guarantee of protection for the following ten years (compare above), a completely successful revaccination may be estimated of like value and treated accordingly. A less persistent effect as regards the duration of the protection has been, either rightly or wrongly, attributed to the

revaccinations with modified (or incomplete) results, and these constitute the majority of all cases. Now, since an excess of caution can harm no one, whereas too little caution may put one or many in danger, I am willing to agree with those who advise a repetition of revaccination after five years, when the last vaccination showed only modified results (Bohn and others). In my own practice I go even further, in that I revaccinate all willing to comply who have not been lately vaccinated, when and as often as the occurrence of variola in the place has been confirmed, and the beginning of an epidemic is possible.

Such precautions seem especially appropriate if the last vaccination took place some time before and proved negative, and the person is consequently under very vague or no definite protection. It is impossible to insist too forcibly or to repeat too often that a negative result proves only that at the moment, and for a short time afterward, there is no susceptibility (compare above), but for the distant future it means nothing. The warning is therefore evident that exactly in such cases there should be no hesitation about a repetition of revaccination, as soon as any reason (the beginning of an epidemic of smallpox) calls for it, and no thoughtless recklessness should be suffered. Finally, if repeated vaccinations were done at not too long intervals, but always failed, the indication for periodic revaccination is less pressing, because it is probable that in these cases the susceptibility has been destroyed; yet simple inaction never does more than is necessary. Much more is repeated revaccination to be recommended in such cases at definite intervals, without attention to the preceding failures or the future results. About five years may be set down as a suitable interval. If this rule is followed, experience teaches that the danger of an intercurrent smallpox infection is reduced to a minimum.

It is scarcely to be expected that so sharp a definition as the above will be taken into consideration by the State in making its laws. Taken in this sense, therefore, the foregoing principles have the empty significance of a longed-for Utopia. Yet the less likely it is that something definite may be accomplished by means of legal force now or later, the more it is and will remain the duty of individual physicians to show its effect by word and action in their own limited circle. For this it is necessary to instruct patients in such a way that they will see for themselves the utility and value of periodically repeated revaccination. The problem is not an easy one, for it appeals more to the clear intelligence than to the feelings of the individual, and daily experience unfortunately teaches us that the

nature of man is such that he can be much more easily persuaded to omit something than be convinced of the utility of something new.

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GENERAL RESULTS OF VACCINATION AND REVACCINATION.

In the preceding sections on Vaccination and Revaccination it was shown how the idea of protective inoculation originated, and what changes this underwent in the course of the nineteenth century. It was further explained what principles are to be maintained in regard to vaccination and revaccination, and how the latter is to be looked on as the necessary complement of the former. We have still to bring forward in a summary way what has been accomplished by both, or, in other words, to name briefly the general results springing from the origin and spread of the procedure.

This can be done, so far as our purpose is concerned, most simply in a deductive way; *i. e.*, by the laying down of a number of principles which modern teaching includes and has concisely expressed.

These principles are based on history; that is, at least, they are to be exemplified by the aid of historic documents. The conclusions of the papers must here suffice, in place of a fuller account, since the amount of material is too great to be communicated *in extenso*.

It has been determined, first, that with the general introduction of protective inoculation smallpox throughout Europe (and likewise outside of Europe) has become much less frequent and less fatal. This conclusion, the most general of all, stands indisputably at the head of the whole inquiry. Since Jenner's epoch-making publications happened to coincide with the opening of the century (1798–1800), and vaccination began with the new century, it may be allowable to say, in a chronological way, that the secular character of variola changed markedly, ameliorated in kind, with its introduction in the nineteenth century. This is evident from the following:

From the time of the middle ages smallpox had taken its part in ever-increasing figures in the statistics of general mortality. Its own

rate of prevalence had finally become excessive. It amounted in the eighteenth century, according to the unanimous statements of contemporaneous writers, to nearly 95% of all the native inhabitants of Europe. This surely occasions surprise, for it affirms in blunt words that on our part of the earth only about 5% of the whole population went through life without being infected. If closely examined, this extraordinary morbidity ceases to appear strange when we consider the intense contagiousness and the viability of the virus, as well as the circumstance that a natural susceptibility to the disease is almost universal in the human species. With the increasing density of the population throughout Europe, and the increasing facilities for travel, it must have eventually come to pass that among the inhabitants of Europe only those few would not be attacked who were endowed by nature with a permanent immunity. (Compare p. 22.)

Another circumstance which especially characterized the conditions at that time deserves mention here. Thanks to the very great danger of infection, which threatened almost every one in consequence of these two phenomena just named (extreme contagiousness and general natural susceptibility), most people were attacked in prevaccination times not so much in adult age as in childhood. Under the existing circumstances only a comparatively very small number could escape, not only entirely, but for any length of time, the prevailing influence of the contagium without being infected, and thereby paying their personal tribute to the demon. The dying, to put it plainly, went hence, never to return. Of those who recovered, the majority, at least, were made immune for the rest of their lives. What remained of susceptible individuals in a place at the expiration of an epidemic constituted, as a rule, so small a portion of the population for the next epidemic that they were scarcely to be weighed in the balance. What did constitute for a subsequent epidemic, occurring sometimes after a short interval, the necessary human material were the young children born in the interval, who had not yet been exposed to the influence of the virus. Variola was accordingly so commonly reckoned as an infantile or puerile affection, that in the consideration of its extrinsic manifestations its intrinsic nature was left in the background; for exceptions to this behavior were seen in Europe only where, on account of a special sterility of the soil, and particularly difficult means of communication, the individual epidemics followed one another at long intervals.

It is worthy of note that variola in prevaccination times, especially

during the eighteenth century, was called in German-speaking countries *Kindspocken* (child-pox), or *Kindsblattern*, being therefore looked on as simply a presumptive disease of childhood.

In that epoch of history, as far as the morbidity of childhood is concerned, smallpox, as a matter of fact, played a similar though disproportionately fatal rôle to our present-day measles. The inferences applied formerly to variola are now applicable to measles, namely, that only the smallest proportion escape infection during life, and the disease is regarded by the laity, with apparent justice, as a disease of childhood, because only a few are in a position to acquire it as adults.

As an example of the behavior of variola formerly, we may mention an epidemic that took place at the termination of prevaccination times which was accurately described by Schwarz. (Compare Juncker, *l. c.*, IV, pp. 33–68.) The epidemic in question occurred in the three cities, Rawicz, Bojanowo, and Sarnowo, in the Prussian province of Posen. Its duration was exactly one year (from December, 1795, to December, 1796). The entire population of the places at the beginning of the epidemic consisted of 13,329 souls, of which within the one year 1252, or 9.4%, were attacked, and 199, or 1.5% of the population and 15.9% of the infected, died. The number of probably susceptible people left at the close of the epidemic was only 524—but a very small percentage, therefore, of the population. The 1252 cases divided themselves among different ages in a characteristic way, as follows:

Between 0 and 5 years...................... 743 persons, or 59.3%
"   5 and 10 "   441   "   " 35.2%

Taking these figures together, we find that between 0 and 10 years 1184 persons, or 94.8%, were attacked, against only 68 persons, or 5.2% (!!), in later life.

In contrast to all this, the nineteenth century showed in its variola morbidity after a few (two or three) decades an entirely different picture. The number of the attacked, which in the previous generation constituted the majority of the living, had decreased to a minimum, and the formerly pronounced disposition of the disease to occur in childhood seemed to have at once disappeared, or, at least, to have decidedly changed.

In regard to this decrease in morbidity, it can now be said without exaggeration (Bohn), as far as central Europe was concerned, that the earlier proportion of the attacked and non-attacked was reversed (5% now, against 95% before), and as to the age predilection, it is now evident that childhood stands decidedly behind adult age. This metamorphosis in the morbidity and behavior of the disease stands unique in the history of infections; and it is impossible that it could

have happened by chance. On the contrary, the origin of so pronounced an alteration presupposes with certainty the entrance of a powerful factor. The appearance of this factor must have occurred at the beginning of the nineteenth century, since the change can be traced to the first decade, and moreover its action must have been such that childhood, even at that epoch, obtained the greatest advantage.

That this factor could only have been vaccination and its general introduction into Europe is obvious to every unprejudiced mind; as a matter of fact, no other determining element is discoverable. A natural diminution in the contagiousness of variola, as well as a natural decrease in the susceptibility of mankind, certainly cannot be excluded. Yet beyond the confines of European civilization, and outside the territories where vaccination is practised, smallpox continues as before to declare itself repeatedly in wide-spread epidemics, and to decimate the population (Steinbrenner, Pruner-Bey, Rigler, Stricker, and others). Moreover, when carefully observed, vaccination of itself appears sufficient to explain the metamorphosis of the disease in Europe, inasmuch as its protective effect, in the countries where it is practised, acts not alone on the vaccinated, but indirectly (by irradiation) on the non-vaccinated. The vaccinated—whose number since the beginning of the century has increased year by year, until now they are reckoned in Europe by millions—were not only rendered immune (for the time being), but also lost the power (again, for the time being) of acting as a center or secondary propagation focus for their vicinity. With the increasing universal spread of vaccination in all European countries which occurred in the first decade of the nineteenth century, not only the number of the immune increased, according to an arithmetic ratio, but the danger of infection for the non-immune decreased in a geometric (or potential) ratio. Both together are more than sufficient to explain the splendid result of the discovery in Europe.

Since, moreover, the vaccination of children became at once the custom, and was soon almost exclusively practised, it is readily intelligible how the reversal of morbidity, spoken of above, occurred. As long as revaccination was not taken up by adults, so long did children, especially the children of those who believed in vaccination, escape the infection in great numbers, for the simple reason that they were still protected by their vaccination.

As an example of this, we may refer to the smallpox epidemic in Würtemberg between 1831 and 1836. In this country the vaccination

of children had been compulsory since 1816 (compare History). Of 100 vaccinated, who were attacked during those years, only 10% were in the first decade of life, while 33.5% were in the second, and 47% in the third. The remaining 9.5% was divided among the other classes (over thirty years of age). Moreover, it is to be noticed that the older people, as a simple calculation will prove, had lived in the prevaccination times, and were therefore, at least the great majority of them, immune from a previous attack (Hein, *l. c.*).

Like the morbidity, the mortality also suffered a marked change with the introduction of vaccination. In the eighteenth century smallpox stood next to pulmonary consumption as the commonest cause of death, for about one-twelfth (on an average, at least 8%) of all deaths was attributed to it.

In the nineteenth century, on the contrary, after the introduction of vaccination, wherever it was practised a striking diminution in the mortality of smallpox (in comparison with the general mortality) occurred. In many places this was already noticeable in the first decade (1800–1810), but with the increasing spread of the new procedure, it sank rapidly until it amounted ordinarily to only 1% or less of the total mortality. A similar favorable result is shown from a comparison of the deaths from smallpox with the number of the population. This gives us figures which, calculated according to the decimal system, must be expressed in fractions of one per thousand. From all this, what we dogmatically stated at the opening of the section follows, that smallpox in the present century has become, for the community at large, much less dangerous than it had previously been.

Statistical proofs from the history of the disease lie before us in numbers. It will be sufficient to subjoin a few of the more important ones:

1. Of greatest importance are the tables of annual mortality from variola in the kingdom of Sweden, to be found in the English "Bluebook on Vaccination." (Compare History.) We have at our disposal from no other country in Europe such comprehensive, and at the same time such accurate, figures as to the mortality from smallpox as these; for they include the long interval from 1774 to 1855. They extend, on the one side, pretty far back into prevaccination times; and, on the other, into an epoch when vaccination (of children) had long been obligatory.

Since vaccination was first performed in Sweden in 1801, but came into general use only in 1810, and was made a legal institution in 1816, the whole interval from 1744 to 1855 may be divided into three natural periods: the first comprehending the prevaccination epoch (1744–1801); the second, the period of transition (1802–1810); and the third, the first forty-five years of the epoch of vaccination (1810–1855). The annual mortality, calculated for every million inhabitants, is as follows:

For the prevaccination period annually..............2050 deaths
  "   " transition period annually .... 686 "
  "   " vaccination period annually................. 169 "

From these figures it is evident that the annual mortality in Sweden, when compared with the entire population, has decreased under the effect of vaccination to about one-twelfth what it was in prevaccination times. In other words, the mortality, which in prevaccination times amounted to more than two per thousand of the population, in the period of vaccination sank to 0.17 per thousand.

2. A further very instructive illustration of the change in mortality in the nineteenth century—that is, under the influence of vaccination—is found in the smallpox statistics of the kingdom of Bohemia, before and after the introduction of vaccination. The Report of the Medical Faculty of the University of Prague (1856), likewise embodied in the English "Blue-book," shows the following figures:

(A) In the seven years immediately preceding the introduction of vaccination (1796–1802) on a yearly average—

The entire population of Bohemia amounted to....3,039,722 people
There died annually .... 94,955 "
  "   "   " of variola.................. 7,663 "

(B) In the twenty-four years after the introduction of compulsory vaccination (1832–1855) on a yearly average—

The entire population of the country was.........4,248,155 people
There died yearly .... 113,412 "
  "   "   " of variola.................... 287 "

According to this, therefore, the ratio of the annual mortality to the entire population in both periods amounted to 1 : 32, or exactly 1 : 32.5, while the ratio of the smallpox mortality to the entire population in period A was 1 : 397, and in period B only 1 : 14,741 (!); further, the ratio of the smallpox mortality to the general mortality in period A was 1 : 12, in period B only 1 : 458 (!).

A still further calculation shows that the ratio of the smallpox mortality to the entire population was 37 times, and the ratio of the smallpox mortality to the general mortality 38 times, more favorable for the period B than for the period A. It is, moreover, interesting to observe that in the seven years of the period A (prevaccination) altogether 55,641 persons died of variola, while in the twenty-four years of the period B (post-vaccination) only 6895 died of this disease. The last figures are about 7.5 times less than the first, although the period B is more than three times as long, and the population of the country in the interval between B and A had increased more than one-third.

3. From the province of Brandenburg (Curmark and Neumark) yearly mortality statistics giving accurate data as to the mortality from smallpox exist since the year 1789, while from the entire Prussian monarchy similar statistics are available only since 1816. Looking first at the prevaccination times, from 1789 to 1799, it is seen that during these the mortality from smallpox amounted to an average of 9.1% of the entire mortality; and in the individual years of the decade in question we see fluctuations between the wide limits of 3.3% and 17.8%, according to the virulence of the *genius epidemicus*.

If we compare with these figures the mortality of variola in the whole of Prussia, for the long post-vaccination period from 1816 to 1870 (inclusive), we find in the latter an average yearly mortality of only 0.8% (!), and the figures for the individual years fluctuate within the relatively small limits of 0.3% and 1.7%. As is at once evident, the latter figures lie entirely outside the former, for their maximum is considerably lower than the former's minimum. Drawing a comparison now between the prevaccination smallpox mortality of the province of Brandenburg, and that of the post-vaccination period for the whole of Prussia, from 1816 to 1870 (naturally, only with reference to percentages), we find that the average percentage of the former is not less than eleven times greater than that of the latter. Moreover, it appears, and this seems worth remarking, that during the post-vaccination period the influence of the *genius epidemicus* on the disease mortality is almost lost, inasmuch as it is not the entire mortality figure that is low, but the fluctuations, as compared with earlier times, are very insignificant. An acute, but fortunately only transitory, change from its customary behavior was seen in 1871 and 1872, during which years the "fastigium" [or acme] of the epidemic that began at the end of 1870 occurred. In these two years the variola mortality in the Prussian kingdom rose again suddenly to 8% of the entire mortality, only to sink back once more immediately afterward. This high percentage for these two years, in its completely isolated elevation, marks for Prussia the severest epidemic of the entire century; yet in spite of this, it does not quite reach the average percentage (for the province of Brandenburg) of the prevaccination period, and is less than the maximal elevation during the same period by more than one-half.

Finally, as further examples of the decrease of the variola mortality following vaccination, two German cities, Berlin and Stuttgart, should be mentioned, since we possess from both accurate figures as to the smallpox mortality in prevaccination times, which can be compared with later conditions:

4. In Berlin, we find from the statistics collected by Guttstadt that in the prevaccination period from 1758 to 1802, the percentage mortality from variola was, on an average, about 8% of the entire mortality, though in individual years when smallpox was severe it repeatedly went above this.

We see, for example:

In 1766	22.1%	In 1789	15.%
In 1770	19.2%	In 1801	21.2%, etc.
In 1786	21.2%		

In the first decade of the nineteenth century vaccination was only passively practised in Berlin (as also in Prussia generally). For this the unfavorable state of the political atmosphere was in a great measure responsible. Consequently, corresponding to this, the percentage mortality from smallpox decreased but little (to 6.7%) in comparison with the entire mortality, though in no single year did it ever go above the previous average of 8.0%.

In the year 1810 vaccination became general in Berlin and Prussia, and at once in the next quinquennium (1810–1814) produced a decrease of the annual percentage mortality to 0.7% (!). During the subsequent long series of quinquennia from 1815 to 1869, the percentage mortality fluctuated between 0.06% and 1.34%, and struck a general average of

0.8%, or exactly one-tenth of that in prevaccination times. Isolated years with severe epidemics (as 1864, with 3.5%) are such rare exceptions as to scarcely deserve notice. But it must be mentioned that in the decade from 1860 to 1870 vaccination in Berlin fell somewhat into disuse, and, as a consequence, a soil was prepared for the pandemic of 1871 and 1872. For these two years the mortality was:

1871 ....15.7% (!)
1872 .... 3.8%

The former percentage seems, to say the least, excessive for the nineteenth century, yet it is decidedly below the above-mentioned maxima for the eighteenth century; the latter, which corresponds to the diminution of the pandemic in Berlin, is almost the same again as that for 1864. (Compare the remark under 3 for Prussia.)

A corresponding fact is evident if the deaths from variola per 100,000 inhabitants in Berlin during the prevaccination times (inclusive of the interval when the conditions were far from perfect, that is, from 1801 to 1809) are compared with those of port-vaccination times up to 1869. There died on an average yearly, per 100,000 inhabitants:

1758–1762	.......407 persons.	1790–1794	......310 persons
1763–1767	......364 "	1795–1799	......239 "
1768–1772	......294 "	1800–1804	......261 "
1773–1784	.......(?)	1805–1809	......306 "
1785–1789	......360 "		

All these figures are characterized, as is readily seen, by their high range.

On the contrary, there died yearly, on an average, from variola in post-vaccination times from 1801 to 1869, per 100,000 inhabitants:

1810–1814	....31 persons	1840–1844	..........13 persons
1815–1819	....40 "	1845–1849	.... 2 "
1820–1824	.... 4 "	1850–1854	.... 5 "
1825–1829	....13 "	1855–1859	..........18 "
1830–1834	....19 "	1860–1864	..........30 "
1835–1839	....18 "	1865–1869	..........26 "

The last two mentioned figures correspond to the previously mentioned neglect of vaccination that occurred in the seventh decade; yet even they remain far below any figures in prevaccination times.

The quinquennium 1870 to 1874, in which the great pandemic fell, requires, naturally, separate consideration. There died during this pandemic in Berlin, per 100,000 inhabitants, a yearly average of 160; a number that considerably exceeds all the previous ones in the same period, yet is much smaller than any in the prevaccination period. (See previous tables.)

5. For Stuttgart (according to Schübler and Cless) the statistics are as follows:

(A) Ratio of the mortality from smallpox to the entire mortality in the years—

1782–1796 ....1 : 13.5
1797–1812 ....1 : 17.1
1813–1827 ....1 : 1148 (!)

(B) Number of deaths from smallpox per 1000 of population in the years—

1782–1796 69
1797–1812 43
1813–1827 .... 0.8 (!)

Vaccination began gradually to be practised in Würtemberg during the first decade of the nineteenth century. In the year 1814 it was provisionally taken in hand by the State, and two years later (1816) was made compulsory for the kingdom. The difference between the mortality in Stuttgart from variola in prevaccination times (1782 to 1786) and that in the above-mentioned post-vaccination period is absolutely astonishing, the former exceeding the latter, calculated according to A, about 88 times; calculated according to B, about 86 times.

The striking decrease in the mortality from variola in the nineteenth century is due to two circumstances, each of which is directly or indirectly the result of vaccination. It came first from the decrease of smallpox morbidity generally, which was partly a direct, partly an irradiated, effect of vaccination *in genere* (see above). The much smaller absolute number of those attacked corresponded naturally to a much smaller absolute number of deaths. In this benefit not only the vaccinated and completely immune participated, but also the non-vaccinated and those who had become again susceptible, inasmuch as the opportunities for infection had lessened in number.

On the other hand, the mortality from variola decreased even more considerably after the introduction of vaccination, on account of the fact that the disease, as it occurred in the vaccinated, was usually much milder than in the non-vaccinated. And this circumstance is of great weight in explaining the diminution of the mortality from smallpox in the nineteenth century; for, taken altogether, the behavior of these epidemics would naturally be correspondingly mitigated, because in them the number of those attacked who had been vaccinated would exceed the number of those who had not been, and consequently the mortality figures from variola in general would be decreased more or less, as compared with former times.

We now come to a second general result of vaccination, which may be briefly stated as follows:

In mixed (*i. e.*, partly vaccinated and partly non-vaccinated) populations the vaccinated are attacked by the disease comparatively less often, and more mildly, and show a considerably smaller relative mortality.

The correctness of this observation is deduced from all the material

that has been collected on the morbidity and the mortality of variola in the vaccinated and non-vaccinated during the nineteenth century.

I commence first with several examples, taken from the practice in hospitals and policlinics, which make one or other of the points in question clear.

1. Among 20,351 hospital patients, whose condition as regards vaccination was exactly known, 1113 were suffering from variola, 19,238 from other diseases. Among the latter 12.7% were not vaccinated; among the former, on the contrary, 41.9%. From this it would follow that the predisposition to variola was three times greater in the non-vaccinated than in the vaccinated (Körösi, *l. c.*).

2. Within the twenty years from 1837 to 1856, altogether 6213 smallpox patients were treated in the General Hospital in Vienna. Of these, 5217 were vaccinated, 996 were not; 1323 suffered from severe variola (variola vera, etc.), 4880 from mild variola (varioloid). These two groups were divided among the vaccinated and non-vaccinated as follows:

Of the 5217 vaccinated, 732, or 14%, were attacked by severe variola; by mild variola, 4485, or 85.9%. While of the 996 non-vaccinated, 591, or 59.3%, suffered severe attacks; 405, or 40%, mild ones. From this we can only conclude that the predisposition to severe variola was 4.2 times greater in the non-vaccinated than in the vaccinated.

3. According to Quincke ("Charité-Annalen," 1855), 1949 smallpox cases were reported in Berlin during the years 1849 to 1853. Of these, 175 non-vaccinated and 188 vaccinated had variola vera, 57 non-vaccinated and 1592 vaccinated had variola modificata (varioloid). The absolute number of the variola vera cases was therefore more than three times greater among the non-vaccinated than among the vaccinated, although the absolute number of vaccinated attacked greatly exceeded that of the non-vaccinated.

Further, of the 1717 vaccinated, 55, or 3.2%, died; of the 232 non-vaccinated, 86, or 37%.

According to this, therefore, the death-rate among the non-vaccinated was twelve times greater than among the vaccinated.

4. In reference likewise to the rate of mortality among the vaccinated and non-vaccinated, Körösi (see above) came in an indirect way to a striking result: Among 13,373 cases that died of other diseases there were 1839 non-vaccinated, or 13.8%. If vaccination was without influence on the death-rate from variola, there should be found among the 1305 deaths from variola occurring at the same time only about 13.8% non-vaccinated. As a matter of fact, the number of non-vaccinated was 1054, or 80.8%. This shows among the non-vaccinated a mortality six times greater than would be expected in other diseases.

5. In the Leipzig Policlinic (according to Thomas) during the epidemic of 1871, altogether 688 smallpox patients were treated. Of these, 417 were vaccinated, with 18 deaths, and 271 were non-vaccinated, with 114 deaths. The mortality among the vaccinated was therefore 4.3% as compared with 42.1% among the non-vaccinated. These percentages stand in the ratio of about 1 : 10 (more exactly, 1 : 9.8), and illustrate

among dispensary patients, as well as in the course of especially wide-spread and malignant epidemics, the immense advantage the vaccinated have over the non-vaccinated, as far as the death-rate is concerned.

These examples from hospitals and policlinics clearly demonstrate that variola affects very differently the vaccinated and the non-vaccinated. Moreover, this difference, as is evident from the facts, extends not less to the susceptibility to infection than to the severity of the attack and the mortality. For further proofs of the correctness of this position, we must refer to the abundance of literature on smallpox and vaccination of the past [nineteenth] century. Yet out of the great mass of material at our disposal, only those communications and papers promise anything for an exact statistical study of the subject in which the vaccinated and non-vaccinated are differentiated, not only in relation to the number of cases and the death-rate from variola, but also in regard to their collective position within the human complex considered at large and without reference to smallpox. From this integral standpoint we find, besides the communication of Körösi (see 1 and 4 above) already mentioned, others from previous and more recent times, some of which we take occasion to refer to:

1. According to the previously quoted Report of the Medical Faculty of the University of Prague (1856), the population of Bohemia during the twenty-one years from 1835 to 1856, according to the official reports, consisted on a yearly average of: Vaccinated, 143,123; non-vaccinated, 4292. Of these, 389 vaccinated and 355 non-vaccinated were attacked by variola on a yearly average. This, therefore, shows infection in the vaccinated in 1 out of 368 persons; in the non-vaccinated, in 1 out of 12. These two figures stand in a ratio to each other of almost 31 to 1, or, in other words, the relative morbidity from variola was for the vaccinated 31 times less than for the non-vaccinated.

The relative mortality stood in the following ratio: During this twenty-one years the average yearly deaths numbered 20 in the vaccinated and 106 among the non-vaccinated. With reference, then, to the entire number of vaccinated and non-vaccinated, there was a death-roll from variola for the vaccinated of 7166 persons, for the non-vaccinated of 41 persons. These last two figures show a relation of 175 : 1, or, in other words, the relative mortality from variola among the vaccinated part of the population was 175 times less than among the non-vaccinated.

Finally, if we estimate the absolute mortality of the vaccinated and non-vaccinated in percentages of those attacked, we find: Of the 389 vaccinated who took smallpox, 20 died, or 5.1%; of 355 non-vaccinated who took the disease, 106, or 29.9%. The mortality among the infected was, therefore, for the vaccinated almost six times less than for the non-vaccinated.

2. At the beginning of the great epidemic of 1870–1871 there were, according to Flinzer, in Chemnitz (Saxony) altogether 64,222 inhabitants, of whom 53,891, or 83.9%, were vaccinated; 5712, or 8.9%, non-vaccin-

ated; and 4652, or 7.3%, who previously had smallpox, none of whom was infected again, and who therefore may be left out of the question.

Altogether, 3596, or 5.6%, of the population were attacked by the disease during the epidemic. Of these, 953 were vaccinated and 2643 non-vaccinated. With reference, again, to the numbers of vaccinated and non-vaccinated actually attacked, there was therefore one case among every 56.7 of the vaccinated, one among every 2.2 of the non-vaccinated. The last two figures bear a ratio to each other of almost 26 : 1; or, in other words, the relative morbidity from variola for the vaccinated was 26 times less than for the non-vaccinated.

The relative mortality was as follows: There died altogether 249 persons, of whom 7 were vaccinated and 242 non-vaccinated. With reference to the entire number of the vaccinated and non-vaccinated, there was, therefore, a death-rate among the vaccinated of 1 in every 7698.7 persons; among the non-vaccinated, of 1 in every 23.6 persons. The last two figures show a ratio to each other of 326 : 1; or, in other words, the relative mortality from variola for the vaccinated part of the population was 326 times less than for the non-vaccinated.

Finally, if we estimate, as in example 1, the absolute mortality of the vaccinated and non-vaccinated in percentages of those attacked, we find:

Of 935 vaccinated who took smallpox, 7, or 0.7%, died; of 2643 non-vaccinated who took the disease, 242, or 9.2%.

The mortality among the infected was, therefore, for the vaccinated almost 13 times less than for the non-vaccinated.

3. A similar condition is seen, according to A. Müller, in the statistics of the city of Waldheim in Saxony during another smallpox epidemic from January, 1872, to April, 1873. The number of the population consisted at the beginning of 5055 persons, of whom 4713, or 93.2%, were vaccinated, 342, or 6.2%, non-vaccinated.

Altogether 250 persons, or 4.9%, were attacked. Of these, 124 were vaccinated, 126 non-vaccinated. There was, therefore, one case among every 38.0 persons vaccinated, one among every 2.2 non-vaccinated. These figures show a ratio to each other of 145 : 1; in other words, the relative morbidity of the vaccinated was 145 times less than that of the non-vaccinated.

The relative mortality was as follows: Altogether 66 persons died, of whom 11 were vaccinated, 55 non-vaccinated. We have here, therefore, a death-rate of 1 in every 428.5 persons vaccinated, and of 1 in 6.2 persons non-vaccinated. These two figures stand in a ratio of 69 : 1; or, in other words, the relative mortality was for the vaccinated part of the population 69 times less than for the non-vaccinated.

If we estimate, again, as in 1 and 2, the absolute mortality of the vaccinated and non-vaccinated in percentages of those attacked, we find:

Of 124 vaccinated who took smallpox, 11, or 8.9%, died; of 126 non-vaccinated who took the disease, 55, or 43.7%.

The mortality among the infected, therefore, for the vaccinated was almost five times less than for the non-vaccinated.

This whole series of examples as to the mortality of smallpox among the non-vaccinated is surely sufficiently convincing that the disease, even in Europe, has lost little or nothing of its malignancy as compared with earlier times. Even now the non-vaccinated suc-

cumb to it, when attacked, in numbers that bear comparison with those of past centuries, since they often reach and also surpass 20% or even 30%.

The doctrine so persistently preached by the opponents of vaccination, and which attributes the lessened mortality from variola in the nineteenth century to the decrease in virulence of the disease, and not to the influence of vaccination, is idle humbug, and, in fact, humbug of the most suspicious kind.

So far in the statements as to the practical results of vaccination not much attention has been paid to the principle of revaccination, because this comes to the front only after what is crudest in the general experience has been disposed of. The decrease in smallpox generally, and its decreasing share in the total mortality in the nineteenth century, as well as its different behavior in the vaccinated and non-vaccinated, first drew the attention of thinking observers to the consideration of revaccination. (Compare History.) Therefore it was but right to discuss all these points in the first instance. Yet the statement of what vaccination has hitherto accomplished is insufficient unless revaccination is also specially brought within the scope of the inquiry, with the view of arriving at an opinion. This shall therefore now be done briefly as follows.

The result of observations on revaccination and their practical significance are expressed in the following conclusion, which constitutes the third and last in relation to our experience in vaccination up to the present.

The revaccinated, that is to say, those effectively revaccinated, succumb to smallpox in cases of infection much less frequently than those who have been vaccinated only once, or who have not been vaccinated at all. Moreover, the danger of infection is much less than in the last two classes. The empiric proofs for this are naturally to be found in greatest numbers where revaccination has been regularly practised for the longest time. We refer now to the armies of those States which for some time have had compulsory vaccination of recruits. Now, if investigation shows that the morbidity and mortality from variola have sunk among these to an uncommonly low level since the introduction of vaccination, and have remained so for some time, while they kept their previous level among the inhabitants generally, the utility of the measure manifestly is proved. The following data show that the above has actually happened:

1. The vaccination of recruits was introduced into Prussia in 1835. In the preceding decade, from 1825 to 1834, the mortality from smallpox

in the army had been not inconsiderable; it amounted altogether to 496 deaths, or 49.6 a year. The number of men in the Prussian army was then much smaller than in later times, a fact that should be taken into consideration. With the introduction of vaccination among the recruits in the year 1835, an extraordinary decrease in the mortality from variola occurred, and this low level has continued in the army without interruption up to the present. The low mortality is shown in the following statistics:

During the subsequent thirty-five years (three decades and the five immediately following separate years) there died from variola in the Prussian army:

1835–1844	altogether	only	.............................39 men
1845–1854	"	"	.............................13 "
1855–1864	"	"	.............................12 "
1865	"	"	.... 1 "
1866	"	"	.... 8 "
1867	"	"	.... 2 "
1868	"	"	.... 1 "
1869	"	"	.... 1 "
1835–1869	altogether	only	.............................77 men

The somewhat higher mortality in the war year 1866 is explained by the fact that, on account of the political complications at that time, some neglect had crept in. All the 8 deaths in this year occurred in non-vaccinated men (Kussmaul, *l. c.*, p. 63).

In general these figures demonstrate that in the entire thirty-five years' space of time following the introduction of revaccination the Prussian army, in spite of the fact that its number had increased, lost in all only 77 men from variola, or six times less than in the ten-year space of time before the introduction of the law (496 men, see above). This surely proves, no doubt after the fashion of *post hoc, propter hoc*, yet all the same clearly, the marvelously favorable influence that the measure in question exercised on the smallpox mortality in the Prussian army.

A comparison of the death-rate from smallpox among the total population of Prussia, which was not placed under compulsory vaccination laws until 1875, with the death-rate in the Prussian army shows striking results in favor of the army if the figures during identical intervals are placed in parallel columns. To demonstrate this, it is sufficient to refer to the decade between 1851 and 1860. During this decade there died:

(A) Among the entire population of Prussia (according to official reports):		(B) In the army (according to Prager, *l. c.*):	
1851	2.179 persons	3	men
1852	3.208 "	1	man
1853	6.734 "	1	"
1854	7.490 "	3	men
1855	1.664 "	0	"
1856	1.270 "	0	"
1857	2.330 "	1	man
1858	4.691 "	0	men
1859	3.530 "	2	"
1860	3.461 "	3	"
1851–1860	36.577 persons	against 14	men

These figures require no further commentary, for they prove, even to the biased, that the portion of the population represented by the army, in reference to its mortality from variola, stood considerably behind the total population. The same is likewise true for all other years, and it is consequently unnecessary to refer to the point further.

Yet in relation to the morbidity from variola, we must mention that during the entire thirty-five-year period from 1835 to 1869 there occurred altogether in the Prussian army only 2982 cases of smallpox, or 93.7 per year. This number is likewise astonishingly small, for it is only about twice as large as the number of deaths from the disease in the ten-year interval preceding the introduction of vaccination among the recruits (49.6). This, then, certainly proves that the danger of infection must also have decidedly decreased for the members of the Prussian army. Finally, in studying the mortality, when we compare the 2982 cases of the disease with the 75 deaths, only 2.2%, we see that by far the great majority of the infections in the army during this long interval must have been mild.

2. Vaccination of recruits became compulsory in the Würtemberg army in 1833, in the Baden army in 1840, and in the Bavarian army in 1844. The reports as to its effects in these three instances are, if possible, even more favorable than in the case of the Prussian army.

In the Würtemberg army, within the twenty-two years from 1848 to 1869, though it increased from 7000 to 9000 men, there occurred altogether only 51 cases of smallpox, and of these not a single one died, while during the same period the entire population of Würtemberg was suffering from repeated wide-spread and malignant epidemics of the disease (Cless, *l. c.*).

As to the Bavarian army, the report of the Minister of War in 1855 (English "Blue-book") shows likewise that from the introduction of vaccination among the recruits (1844) no single death from variola had taken place.

Finally, in the Baden army, the number of which rose, during the interval, from 7000 to 10,900 men, there occurred, from 1840 (the time of introduction of vaccination among the recruits) to 1869 inclusive, only two deaths altogether from variola (one in 1840, the other in 1859); all the other cases of smallpox in the army (359 in thirty-nine years, or 9.2 per year) recovered; while in the thirteen years before the introduction of vaccination among the recruits (1827 to 1839) there occurred in the Baden army, which was then much less in number (consisting of about 4500 men), 11 deaths from variola (Kussmaul, *l. c.*). All these instances, not excepting the last, demonstrate convincingly the benefit accruing to the different armies from revaccination.

Finally, the same is true of the Hanoverian army, and of the armies and navies of Sweden, Norway, and Denmark (Kussmaul).

Taking up the problem of the protective value of revaccination, the question arises as to its practical results. Experience in regard to this so far teaches us first that the successfully revaccinated possess a general advantage over the non-vaccinated (inasmuch as they are more immune, suffer less frequently from severe attacks of the disease, and, finally, show a decidedly less mortality); secondly, that the successfully revaccinated likewise possess an advantage over the

unsuccessfully revaccinated. To illustrate these two positions, I will refer to a few striking examples:

1. In the Baden army between 1840 and 1868, altogether 100,546 revaccinations were done; 40,040, or 39.8%, of these successfully (Kussmaul). During the thirty-nine-year interval 359 cases of smallpox, as mentioned before, occurred in the Baden army. Of these, only 34 were in the successfully revaccinated, while 325 were in the non-vaccinated, or at least in the unsuccessfully revaccinated.

These figures are an evident proof of the value of successful revaccination, otherwise the number of cases in the successfully revaccinated would have been much higher. True, these figures give no direct comparison as to the morbidity among the successfully and unsuccessfully revaccinated, because the latter are bracketed with the non-revaccinated.

2. There occurred in the Prussian army during the two years 1866 and 1867 (according to Prager, *l. c.*), 320 cases of variola, of which 10 (or 3.2%) died. All these deaths occurred in the non-vaccinated. According to the character of the disease, there were 295 cases of mild variola (variola modificata) and 25 of severe variola (variola vera). Of the latter, 24 occurred in the non-revaccinated and one in an unsuccessfully revaccinated. The whole 320 cases divided themselves as follows:

In the non-revaccinated.....................185 cases, or 57.8%
In the unsuccessfully revaccinated........... 73 " " 22.8%
In the successfully revaccinated............. 63 " " 19.8%

It is consequently evident that the successfully revaccinated possess the greatest advantage, for among these statistics they show no mortality, no instances of severe variola, and the smallest percentage of cases generally.

After them come the unsuccessfully revaccinated, showing somewhat less favorable figures, and, finally, separated from both by a broad chasm, come the non-revaccinated, who show the entire mortality, almost all the cases of variola vera, and more than half the cases of infection generally.

How much is to be attributed to regular revaccination, and what effect it may exercise at the time of extreme wide-spread danger, was shown most strikingly in the Franco-Prussian war of 1870–71, during which the greatest epidemic of smallpox of recent times broke out. Here were the two great armies of two military nations under decidedly unlike conditions so far as vaccination, and especially revaccination, were concerned, and here was seen in a marked way the relative advantage on the side of the Germans. It is impossible to say more than the "relative" advantage, for we cannot conceal that the German soldiers too suffered, on account of the exceptional conditions under which they were placed, a loss from variola that far surpassed anything of all the other preceding decades. Yet these figures appear truly insignificant in comparison with the losses in the French army, and likewise small in comparison with those of the general population

of Germany. We therefore introduce them as a striking example of the utility of revaccination:

The German field-army (with a strength of more than a million men) offered during the war of almost one year's duration to the pandemic only 4991 cases of smallpox in all, although it found itself in France in the midst of a population that was suffering severely from the disease. Of the attacked, only 297 died, making a mortality of 5.97%. Of the German troops that remained stationary during the same time, 3472 were infected, of whom 162, or 4.60%, died. Altogether, then, 8463 men were attacked, of whom 459, or 5.42%, died.

The French army lost, on the other hand, by death (*Wiener med. Wochenschr.*, 1872, S. 896) the immense number of 23,469 men, or 49 times more than the loss on the German side (see p. 183). The total number of cases in the French army is not accurately known, so that the rate of mortality cannot be calculated. Yet for the portion of the French army, consisting of 372,918 men, that were made prisoners of war, the rate of mortality has been determined. This amounted to 13% of the attacked (1963 deaths), or more than double that of the German army. (Compare again p. 183.) How severely single divisions of the French army suffered from variola during the war is shown, among others, by the instance of the garrison of Langres, that consisted of 15,000 men. In the never closely besieged fortress, which was merely "observed by the enemy," not less than 334 men of this garrison died of smallpox within seven months (September, 1870, to March, 1871); while the mortality in the whole Prussian army (amounting to at least 450,000) during the whole eleven and a half months of activity was only 316 men.

In other words, that single French garrison, numbering 36 times less, lost in a considerably shorter time (seven months as compared with eleven and one-half months) more cases by death than the whole Prussian army during the entire war (Lotz, *l. c.*, p. 98).

Moreover, the rate of mortality from variola in the German army appears very favorable when contrasted with that of the inhabitants of Germany generally; as, for instance, 459 deaths among the (mobilized and immobilized) troops, in contrast to 59,839 deaths in the Prussian kingdom in the year 1871; and even more favorable when contrasted with the 5508 deaths in Berlin (in the same year), the population of which was then only 826,341, or much less than the number of men in the German army. The devastation that the disease effected during the same year among the inhabitants of France deserves more careful consideration.

An attempt was made to explain away the disproportionately great loss from variola which the French army suffered during the war and to obscure the true causes of the same by the allegation that the men were depressed, mentally and physically, by the continual defeats, and consequently were less resistant to infectious diseases. This argument is very weak, for it is well known that during the preceding years of peace the mortality from variola in the French army was much greater than, for example, in the Prussian army. The war, therefore, only increased the conditions that were already existent.

In the four years of peace, 1866 to 1869, preceding the outbreak of the war the French army lost 380 men from variola, and in the year 1869 alone 63, while the Prussian army in the thirty-five years after the introduction of compulsory revaccination (1835 to 1869) lost altogether only 77 men (Lotz, *l. c.*, p. 97). This alone is sufficient to show the erroneousness of the explanation mentioned above, even when the average strengths of the armies are taken into consideration; for from 1866 to 1869 the French army numbered 383,177 men, while the Prussian counted 248,746, or only about one-third less.

The erroneousness of that conclusion is, moreover, again shown by the fact that the immunity of the German troops, in contrast to that of the French, appeared only in the case of variola, not in other infectious diseases, as, for instance, dysentery or typhoid fever. The German soldiers, who were obliged to live also under by no means the best hygienic conditions, in spite of the confidence inspired by victory, suffered and died from these other infectious diseases, not only in like, but often in greater, numbers than many of the French troops. Therefore there can be no doubt that the exclusive immunity of the German army to variola can be referred only to the well-arranged and vigorously enforced revaccination laws.

If the death-rate from variola, dysentery, and typhoid fever in the Prussian army is compared with the same in the previously mentioned garrison of Langres, in both of which bodies of troops these three diseases were epidemic during the siege, we find the following (Lotz, *l. c.*, p. 98):

THERE DIED PER 10,000 MEN:

In the Prussian army:		In the French garrison of Langres:
From variola	5.8 men	222.6 men (see above)
" dysentery	32.3 "	19.3 "
" typhoid fever........	118.8 "	80.6 "

These statistics show that the mortality from dysentery and typhoid was considerably greater in the Prussian army than in the French garrison of Langres, while in reference to variola the opposite is seen in a high degree.

Finally, the actual results of the German revaccination law remain to be considered, since this is of especial value in the discussion of the utility of revaccination. This law, the wholesome effect of the last great smallpox scare, commands, as is well known, a revaccination every twelve years (particular exceptions omitted) for all the inhabitants of the German empire, and was put in force (compare p. 184) on April 1, 1875. So far it has been carried out on the part of the State with praiseworthy energy and exactness. We should therefore be allowed to refer the alterations in the behavior of variola to this law and its proper management. The results speak so decidedly in favor

of revaccination that we cannot pass over them. They serve rather as unqualified than as strong proofs for the belief that in the proper carrying-out of this principle lies the true means of prophylaxis. This is most evident from the mortality statistics of variola in Germany since 1875, which the Imperial Board of Health gives as follows:

1. The mortality from variola in Prussia within the years from 1816 to 1870, calculated per 100,000 inhabitants, fluctuated between 7.32 and 62.0 per year, and although large enough, was small compared with earlier times (compare above). The disastrous years 1871 and 1872 gave a new buoyancy to the disease, so that the death-rate jumped at once to 243.20 and 262.67, respectively.

On the contrary, from 1875 to 1886 the yearly mortality for Prussia amounted to 3.6 as a maximum (1877), and struck a general average for the twelve years of 1.91. These figures show most clearly the very considerable and permanent decrease of the death-rate after the introduction of the new law into Prussia, the largest of the States in the German empire.

Austria may serve as a contrast, in which the lax vaccination and revaccination conditions continued almost unchanged, even after the great pandemic:

2. In Austria during the years 1848 to 1871, the yearly variola rate of mortality, calculated per 100,000 inhabitants, fluctuated between 15.7 and 84.7; during the years of the pandemic (1872 to 1874) it increased to 189.99, 323.36, and 187.73 respectively. In the following decade, from 1875 to 1884, a remarkably low level was reached in comparison with the previous frightful excess, yet in this decade the death-rate remained always between 39.28 (1876) and 94.79 (1882) per year, or at a higher average than even between the years 1848 and 1871 before the outbreak of the pandemic.

These figures show unequivocally that, in contrast to the behavior of the disease in Prussia, there was no trace of a decrease in mortality after 1875 in Austria; therefore they prove indirectly, though none the less absolutely, that this decrease in mortality in Prussia must be referred to the carrying-out of revaccination.

3. It is instructive to compare the mortality from smallpox since 1875 in the five large German cities, Berlin, Hamburg, Breslau, Munich, and Dresden, with that of four large cities outside of Germany—Paris, St. Petersburg, Vienna, and Prague. During the first decade after the introduction of revaccination (1875–1884) there died from variola on a yearly average, per 100,000 inhabitants:

In Berlin only .... 1.16 persons
" Hamburg only................................ 0.74 person
" Breslau   " .... 1.11 persons
" Munich   " .... 1 45   "
" Dresden   " .... 1.03   "

While within the same time the rates were:

In Paris .... 26.24 persons
" St. Petersburg .... 35.82   "
" Vienna .... 64.90   "
" Prague ....147.90   "

or, further, the maximum and minimum were:

In Berlin	5.19 (1875)	0.10 (2 different years)
" Hamburg	3.58 (1886)	0.00 (6 different years)
" Breslau	8.34 (1883)	0.00 (7 different years)
" Munich	10.30 (1881)	0.00 (6 different years)
" Dresden	3.36 (1880)	0.00 (5 different years)

while the maximum and minimum were:

In Paris	108.91 (1880)	3.60 (1884)
" St. Petersburg	144.91 (1878)	0.00 (3 different years)
" Vienna	167.80 (1876)	1.60 (1889)
" Prague	349.78 (1877)	10.92 (1875)

From these figures it is clear that the rate of mortality from smallpox in the largest cities in Germany, in contrast to Paris, St. Petersburg, Vienna, and Prague, since 1875, is exceedingly small.

That these differences in mortality are not limited to the large cities within and outside Germany, the following shows:

4. If we estimate the average rate of mortality from variola in the German cities with 15,000 inhabitants and over at 1, then for the single years from 1886 to 1889 it amounted to:

In the cities of:	1886.	1887.	1888.	1889.
France	81	92	136	91
Hungary	607	322	30	222
England	19	9	16	6

5. From a very recent communication (1896) of the German Imperial Board of Health to the German Reichstag, we learn that for the years 1886 to 1891 the annual death-rate from variola amounted on an average to 126 throughout the German empire; and, further, that when calculated per 1,000,000 inhabitants from 1889 to 1893, only 2.3 persons a year died in Germany, while, calculated in the same way, the French cities showed a death-rate per year of 147 persons, Belgium of 252.9, Austria of 313.4, and Russia (from 1891 to 1893) of 836.4. If the mortality in Germany had been as great as in these countries, there would have been (instead of only 126) no less than 7321 deaths, or 12.584, 15.543, and 41.854 deaths per year per million of inhabitants.

With the advent of compulsory revaccination in the twelfth year, the revaccination of recruits in the German army lost none of its strictness, and to it all who enter the army must submit. Corresponding to this, the mortality in the German army from variola, which was already very small, has sunk to a minimum, while in the large armies with lax vaccination regulations, as, for instance, the French and Austrian, the figures still remain high:

There died altogether in the German army from variola during the thirteen years from 1875 to 1887 only one (and this one an unsuccessfully revaccinated reserve who was brought in for a drill); while in the French

army from 1875 to 1886 there died 550 men, or 45.8 per year; and in the Austrian army from 1875 to 1881, 595 men, or 85.0 per year.

With the decrease in mortality since 1875, a decrease in morbidity has gone hand in hand. This is very clearly illustrated when we compare the present conditions in the German army with those of earlier times, and with those of other armies. We will content ourselves with the following figures:

Calculated per 100,000 men, variola attacked in the German army per year:

1867–1869	38.7– 74.2	men
1870–1871	565.7–684.2	"
1872	161.35	"
1873–1883 only	2.2– 8.3	"
1883–1887 "	1.8– 20.7	"

while in the Austrian army, smallpox attacked in:

	1870	687.3	men
	1871	815.8	"
Pandemic {	1872	1789.0	"
	1873	1658.0	"
	1874	1003.0	"
	1875–1879	274.0–412.0	"
	1880–1886	140.1–475.3	"

and in the French army:

1867–1869	231.14–632.99	men
1875–1881	111.2 –230.47	"

(Peiper, *l. c.*, p. 74.)

Finally, the total number of cases in the German, Austrian and French

great, has since 1875 become striking.

Finally, under the present conditions in the German empire, we may now justly be allowed to affirm that variola has become, since 1875, an exotic disease in German territory; for the great majority of all cases that have occurred since then have been located at the outskirts of the empire, and not in the interior. Moreover, the disease was found particularly in persons who had come from neighboring countries, and who had apparently carried the germ with them. These circumstances likewise show the blessing of the new Imperial Vaccination Law and its stringent revaccination provisions.

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1875–1881	....	111.2 –230.47 "

(Peiper, *l. c.*, p. 74.)

Finally, the total number of cases in the German, Austrian, and French armies amounted to:

In the German army	(1875–1887)	.............14.8	men
" " Austrian "	(1875–1886)	.............10.238	"
" " French "	(1875–1881)	.... 5.605	"

The difference in morbidity in favor of the German army, previously great, has since 1875 become striking.

Finally, under the present conditions in the German empire, we may now justly be allowed to affirm that variola has become, since 1875, an exotic disease in German territory; for the great majority of all cases that have occurred since then have been located at the outskirts of the empire, and not in the interior. Moreover, the disease was found particularly in persons who had come from neighboring countries, and who had apparently carried the germ with them. These circumstances likewise show the blessing of the new Imperial Vaccination Law and its stringent revaccination provisions.

From 1886 to 1889 in Germany the death-rate from variola was:

	At the frontiers:	In the interior:	Altogether:
1886	110 cases	45 cases	155 cases
1887	119 "	49 "	168 "
1888	94 "	16 "	110 "
1889	188 "	12 "	200 "

The foregoing synopsis of the practical results of vaccination and revaccination as protective measures against human smallpox is by no means complete, since, as far as empiric proofs were concerned, we were obliged to limit ourselves to isolated examples; yet what we have brought forward is more than sufficient to show the mighty revolution that has been accomplished by Jenner and the continuation of his work in the prophylaxis of variola.

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IRREGULARITIES IN THE COURSE OF VACCINIA. COMPLICATIONS AND SEQUELS.

The course of *vaccinia humana* in case of vaccination or revaccination sometimes shows deviations from its ordinary or normal behavior. These irregularities are qualitative in character, and occur only exceptionally; for under this heading we do not include the modified or rudimentary forms of the disease, already described as vaccinoid, since they differ from the perfect results only quantita-

tively (or in intensity), and in the repeatedly vaccinated are the more common. Among the irregular forms the following may especially be numbered:

1. *Vaccinæ bullosæ s. pemphigoides* constitute a rare anomaly of development, in the course of which, on the second or third day instead of normal papules, vesicles with a pemphigus-like aspect make their appearance. These vesicles tend to break down and become converted into ulcers, which are covered with thin yellowish crusts. The contents of these vesicles are, contrary to those of normal vaccinia, not reinoculable; moreover, as far as our experience goes, they do not produce in the individual immunity from variola or vaccinia. When they heal, no scars remain. *Vaccinæ bullosæ* apparently represent a premature degeneration of the vaccine, by which the virus is in some way or other destroyed. The cause of this anomaly, which sometimes occurs only sporadically, but sometimes also in endemic or epidemic form (Zöhrer), is entirely unknown.

2. *Vaccine ulcer (vaccinæ ulcerosæ)* is the conversion of the developing papule, which up to this time was normal, and should now dry up and form a scab, into a suppurating open ulcer of varying depth and breadth. The external cause of this undesirable occurrence is usually maltreatment of the developing or mature vaccinia by scratching, so that apparently a mixed infection of ubiquitous pathogenic micro-organisms takes place.

These ulcers ordinarily run a sluggish course, show a tendency to the formation of fungous granulations that bleed easily, and leave behind lasting scars. They are most frequently met with in those cases of vaccinia which run a course with marked inflammatory symptoms, and, on account of the irritative subjective sensations, lead to scratching, rubbing, etc.

Since these ulcerous processes begin only after the vaccinia has advanced to such a stage that its results are assured, they have no influence on those results. Yet they render a special treatment necessary (by the ordinary remedies).

3. Sometimes, but fortunately rarely, the pustule becomes gangrenous (*vaccinæ gangrænosæ*) and covered with a black, evil-smelling slough. This anomaly is seen only in isolated cases in run-down individuals (especially in neglected and miserable foundlings). Its treatment is that of gangrene generally.

4. In some instances the contents of the papule during development, or after it has become a pustule, become hemorrhagic (*vaccinæ hæmorrhagicæ*). These hemorrhagic vaccinia pocks are the mor-

phologic analogues of hemorrhagic variola. Usually the signs of a hemorrhagic diathesis are found. (See "Complications," following.)

Besides these anomalies that are observed in the papule, there are others which must be considered, such as pathologic processes in the skin of great and sometimes universal extent, which now and then develop during the course of the vaccinia or at its close, and which, in the narrow sense of the word, are of the nature of a complication. Among these we mention, first, the different kinds of eczema—moist or dry, vesicular, pustular, or sometimes even bullous (Bernouilli and Schneider). In some such cases the impression is as if the peculiar predisposition to skin eruptions (eczema, impetigo, etc.) was, under particular circumstances, especially in scrofulous individuals (children), awakened and stimulated by the local effects of the vaccination (F. von Niemeyer); yet in other cases, and especially where the condition is the so-called acute universal eczema, it seems more likely that it may be due to a particular kind of infection conveyed by means of the vaccination.

The course of this post-vaccinal eczema, which never threatens life, may be acute, or, again, more chronic. Its treatment is according to the diagnosis of its origin, sometimes purely local, but again constitutional (treatment of scrofula).

Among the most important and relatively most frequent complications of vaccinia is erysipelas. This is always serious, and may even threaten the life of the individual. It may show itself as a complication at any stage in the progress of vaccinia, though it most frequently manifests itself on the second or third day after the inoculation. This point of time falls, according to our earlier description (compare p. 199), either in the latent stage, or, at the latest, in the beginning (therefore primordial) stage of development. When it occurs early in vaccinated persons and develops from the site of vaccination, we are justified in speaking of vaccination erysipelas (*erysipelas vaccinatum*); that is, in referring the origin of the erysipelas directly to the vaccination.

For, according to Fehleisen, the origin of erysipelas is due to an infection with streptococci, which produces the specific disease locally after a short latent period (of one or two days), and it cannot be doubted that in this case the introduction of the streptococci occurred through the vaccination. Employment of lymph containing streptococci, or the use of imperfectly disinfected instruments, unclean hands, the performance of the operation in an infected place, a questionable condition of the linen of the patient, may be responsible for the origin

of the disease.   It sometimes occurs sporadically, but again epidemically.

Vaccination erysipelas usually runs a course with high fever, accompanied by the other severe general symptoms [of the traumatic form of erysipelas].   As far as the skin lesions are concerned, they may be of varied extent and intensity, and may show the well-known tendency to "wander" or "migrate."   A more detailed description is here unnecessary, inasmuch as its symptoms do not differ from those of wound erysipelas generally.

But it is important, in relation to the question of vaccinal protection, to say that the vaccination is usually unsuccessful, the site of inoculation remaining sterile or suppurating prematurely, so that the prophylactic effect of the vaccination not seldom becomes questionable, owing to both causes.

Fatal cases are not uncommon, at least in comparison with the number of cases.   The prognosis must therefore be considered to be at least dubious.   Besides this form of erysipelas, which occurs early, there is another, which occurs late; and under this designation of "late erysipelas" are included all the cases that occur, not during the first days after the vaccination, but any time afterward, during the course of the vaccinia.   Since this form also commonly originates at the site of the vaccination, it is impossible not to attribute the origin to a subsequent infection of this site.   Such an infection may take place if the developing vaccinia is mechanically injured or breaks open spontaneously, if the scab loosens or is pulled off prematurely—in short, if disturbances of continuity (excoriations or ulcers) occur by which the exciting cause of erysipelas may enter.   Such an excitant, in the form of either Fehleisen's or Rosenbach's streptococcus, must be present before the erysipelas can arise.   The occurrence of this complication therefore depends on the existence of this organism in the immediate neighborhood of the subject of vaccination in each separate case.

Late erysipelas, the symptoms of which do not differ in any important way from those of wound erysipelas, must not be confounded with the rash-like erythema vaccinosum (compare p. 203) that sometimes occurs eight or nine days after the inoculation.

This is a clinical analogue of the corresponding prodromal exanthem of variola, and has nothing to do with exudative inflammation of the skin.   And it is to be remembered that with the appearance of suppuration on the eighth day in a successful vaccination a characteristic inflammatory-congestive area normally arises around

Jenner's vesicle, which morphologically takes on a sharply limited margin (erythema marginatum) like erysipelas, and yet is to be explained otherwise.

It remains a suitable problem for future bacteriologic investigation to clear up the point whether or in how far this normal occurrence in the course of vaccinia has anything to do with a mixed infection. (Compare p. 33, on "Variola," Etiology, under Parasitology of the Smallpox Virus.)

The prophylaxis of vaccination erysipelas demands the strictest precautions in the choice of the inoculated material (lymph or pulp), about which everything necessary has already been said in the section on the Hygiene and Technique of Vaccination.

The question whether animal lymph, on account of the insusceptibility of calves to erysipelas, gives a greater guarantee against the complication than human lymph must be left to the future to decide; *à priori* it appears as if it would give greater security. Asepsis, however, in the operation is the surest means of avoiding erysipelas, and for this we must refer to the corresponding section. Moreover the whole course of the vaccinia requires attention to all precautions that might prevent traumatism, or contamination of the site or its surroundings. Only when all requirements are met is our duty fully done and a guarantee given that nothing important in regard to these complications has been omitted. In general it is not to be denied that vaccination erysipelas, of both forms, has been recently seen more rarely than in earlier times. This is unquestionably to be attributed to the more thorough carrying out of the necessary prophylaxis.

The treatment of vaccination erysipelas is the same as that of erysipelas generally. I refer, therefore, to the corresponding section of this text-book.

Much more rarely than erysipelas do we see phlegmon, lymphangitis, phlebitis of the veins of the arms, suppuration of the axillary glands, and purulent metastases to different parts (as an expression of true pyosepticemia). There is naturally here on every occasion, either with the vaccination or after it, an accessory infection with the corresponding micro-organisms (*Staphylococcus pyogenes aureus, Streptococcus pyogenes Rosenbach, Bacillus septicæmiæ*, etc.).

Somewhat more frequently as a sequela, furunculosis is observed, which is always attributable to a staphylococcus invasion of the blood-vessels. As to the prophylaxis of all these complications, the same is to be said as in the case of erysipelas—namely, thorough asepsis in the operation, proper treatment afterward. The curative treatment of these conditions also requires no particular explanation.

A peculiar infectious disease associated with fever, impetigo contagiosa, has recently (since 1885) attracted the attention of vaccine physicians, since it has been observed several times epidemically among the newly vaccinated, though usually simultaneously among the non-vaccinated also (epidemics of Wittow, the Island of Rügen, of Schlawe and Meseritz, of Cleve, etc.). It appears to be a contagious process, the virus of which has not been absolutely determined (according to Pogge, staphylococci?).

A more detailed description of the affection would be out of place here. Its prognosis is in general favorable, although isolated deaths have occurred. In reference to the prophylaxis, it is clear that it corresponds with that of erysipelas and the other infectious complications.

Herpes circinatus has been observed several times after vaccination done with calf's lymph. Considering the frequency of the *Trichophyton tonsurans* in horned cattle, it is not surprising that accidental transference should now and then occur, though greater care on the part of the physician would prevent it.

A combination of vaccinia with the hemorrhagic diathesis has been observed at different times, expressed in different ways. In some of the cases (Henoch, Strohmayer, Bergeron, and others) there was hemophilia, the existence of which was known previously, or subsequently established by the occurrence of dangerous (even fatal) hemorrhage from the site of vaccination immediately following the operation. It is well known that a wound of the corium by the lancet, like any injury to the vascular layer of the skin, may lead in a bleeder to a hemorrhage that is difficult or impossible to stop; from a symptomatic point of view, this acts as the principal criterion of the disease.

As to prophylaxis, the advice mentioned in another connection on page 196 is applicable here, namely, in hemophilics, or those who are suspicious, to do the vaccination with especial care, if it is done at all. Since in the operation an injury to the corium is unnecessary, care should be taken in these cases, when possible, that the lancet does not penetrate the deeper layers of the epidermis.

Severe and dangerous hemorrhages, as a direct result of the vaccination trauma, have occurred in isolated cases of other hemorrhagic diseases, as, for instance, leukemia (Pott). As in the previous cases, there is no doubt that in these, the hemorrhagic diathesis already existed, and that, not the inoculation of the vaccine virus, but rather the trauma necessarily associated with the vaccination, is to be held responsible for the hemorrhage.

In other cases the hemorrhagic diathesis became conspicuous in other ways. Among these are to be reckoned especially the numerous epidemic occurrences of a general hemorrhagic diathesis in the vaccinated (and non-vaccinated) such as were observed during the American Civil War, in the prisons of the South (especially in Georgia) (L. Pfeiffer).

Since the majority of these cases bore the stamp of an outspoken cachexia, it is likely that we have to do with a true scurvy, which might have been acquired just previous to, or have shown itself for the first time after, the vaccination (perhaps provoked by the latter). Since recent experience points more and more toward scurvy being a specific infectious disease, the possibility of the transference of it by vaccination is by no means excluded.

Finally, some sporadic cases observed of late years should be mentioned, in which the hemorrhagic diathesis appeared as a complication subsequent to the vaccinia. In their clinical symptoms these cases resembled most the so-called purpura, and possibly there was in them some specific virus that was conveyed by means of the vaccination, or became effective simultaneously with it. Yet this is a pure conjecture, for which there are no proofs, as is likewise the conclusion that they might have been instances of scurvy. In reference to the behavior of the vaccine pock, these cases showed differences from one another; for while in some (as in the observations of Fickert, Gregory, Burdereaux, W. Koch) the hemorrhagic complication was first remarked in the papule, the contents of which became bloody, and only subsequently hemorrhagic symptoms (as petechiæ and ecchymoses of the skin, epistaxis, bleeding from gums, hematuria, etc.) appeared elsewhere; in others (as in Epstein's two cases) the vaccine pock itself showed no hemorrhagic change and the general diathesis manifested itself in other parts. This difference gives not the least clue as to the nature or origin of the hemorrhagic complication, and is really extraneous to the matter in hand, yet since it has been noticed, we took occasion to mention it.

The prognosis of vaccinia complicated by the hemorrhagic diathesis is always dubious, no matter to what class of hemorrhagic diseases the complication belongs. The seriousness of the situation lies in the general character of the individual affection, which on clinical grounds also should be differentiated. The treatment is symptomatic.

Other acute diseases, as, for instance, the acute exanthemata, like measles, scarlet fever, and varicella, have been repeatedly observed as complications of vaccinia. These complications naturally depend

on the accidental coincidence of two different pathologic conditions. As to the coincidence of variola with vaccinia, and their remarkable concurrent course, all that need be said has been already mentioned in its proper place. (See pages 205 *et seq.*)

Among the chronic conditions that are to be mentioned as bearing a relation to vaccination, syphilis occupies the first place; in fact, the first place among all the complications that occur with vaccinia generally, both practically and theoretically.

We will first consider the behavior of vaccinia in syphilitics, although, as a rule, it shows nothing extraordinary. If an individual (child or adult) with latent or manifest syphilis is vaccinated or revaccinated with normal vaccine, and the inoculation is successful, the development of the vaccinia is distinguished in no way from that in non-syphilitic persons. Especially in those vaccinated for the first time, Jenner's vesicle may appear most typical, and the further progress of the vaccination (the suppuration, the desiccation, the scar-formation) usually likewise shows nothing abnormal. We may say, then, that in general syphilitics react to the vaccine virus exactly the same as non-syphilitics, and that to the naked eye there is nothing to indicate whether the patient is a syphilitic or not.

But if, on the contrary, vaccine material is taken from a syphilitic for the purpose of vaccinating another non-syphilitic individual, besides the vaccinia, syphilis also may be transferred; and, in case the patient is insusceptible to the vaccinia, syphilis alone. Such a syphilis acquired by means of vaccination is designated vaccination syphilis (*syphilis per vaccinationem s. syphilis vaccinata*).

The earliest reports of syphilis following vaccination come from the first decade of the nineteenth century (Moseley), yet these are not absolutely proved. In 1814 Monteggia, in a communication to the Academy at Milan, affirmed that the vaccine pustule of a syphilitic contained the virus of both syphilis and vaccinia, both of which might be inoculated. This view did not meet with very general acceptance. In the following decade the observations increased in number so that the " post hoc " conditions were made more certain and the idea of a " propter hoc " gained in probability.

Yet the possibility of the communication of syphilis by vaccination remained in the arena of scientific controversy for a long time, and the etiologic connection of the two was positively denied by many on theoretic as well as on empiric grounds. A glance into the contents of the English "Blue-book" shows, for instance, that at the time of its publication the opinions of otherwise competent authorities differed

widely on the subject, and that the majority of them would not allow its possibility.

Among the reasons advanced at that time against the theoretic possibility of vaccination syphilis is to be mentioned the well-known (though false) doctrine of Ricord, according to which syphilis that has become constitutional (including even the primary lesion, the so-called hard chancre) is no longer transferable; naturally, therefore, syphilis in whatever form it existed could not be conveyed through vaccination.

Not only Ricord himself, but, following him, a great number of medical authorities in all countries, suffered in reputation by the downfall of this doctrine. With the proof of its falseness fell one of the principal objections to the possible existence of vaccination syphilis. Another *à priori* reason was based on the fictitious idea that in a typical Jenner vesicle it was impossible for any other contagium besides the vaccinia to be present. Therefore the transference of syphilis from genuine Jenner vesicles was inconceivable. This opinion was diametrically opposed to that of Monteggia, who had even so positively affirmed such a double virus to exist in the vaccinia of syphilitics, yet very many were convinced. Only with the origin of the dual theory of syphilis itself did this lose its principal value in relation to vaccinia, since this showed an analogy between the two. Besides these theoretic objections, which fell to the ground one after another, others, the result of practical experience, were advanced in opposition to syphilis vaccinata, inasmuch as a whole series of premeditated inoculations with the contents of a Jenner's vesicle from syphilitic patients always showed as a result vaccinia alone, and never a subsequent syphilis (Bidart, Montain, Schreir, Heim, Bousquet, and others). Further, it appears even yet very remarkable, and it in some degree defies an intelligible explanation, why, among the actual multitude of diseases resulting in those lately infected by syphilis, syphilis did not follow in all the members of this group of infections. Even though the gradually increasing partizans of the doctrine of vaccination syphilis eventually prove their position, there will still remain questions to answer. This much is at least evident from the observations, that syphilis does not necessarily follow, even when the vaccinia is taken from a syphilitic source (compare below).

In our day the question of syphilis vaccinata is definitely settled in the affirmative; yet it has also been determined that not all cases of syphilis following vaccination are cases of vaccination syphilis. Among the grounds which at present serve as a proof of the existence of syphilis vaccinata is first to be mentioned the result of an entirely unprejudiced numeric study of a very large number of grave occurrences of this kind. If, as Köbner found, among 324 persons vaccinated from suspicious sources, not less than 222 had acquired, after vaccination, the self-same other disease, namely, syphilis, the conjecture is very likely that this was not a mere coincidence. And when, further, these observations have been collected, not so much from isolated cases, as from groups of cases, the mathematic proba-

bility is considerably increased that the cause is to be referred to the single suspicious source from which the vaccine material, directly or indirectly, came.

Moreover, the concrete probability of a causal connection is greater, the larger the numbers are in which the cases grouped themselves (Depaul).

The literature of vaccination syphilis shows in this regard many proofs, of which I abstract a few:

The first well-known announcement of the occurrence of syphilis in a number of cases after vaccination was made by Marcolini (in Udine, 1814). From one girl 10 children were directly inoculated; and from the latter 30 more. A "considerable number" of these 40 children developed syphilis, and some communicated the disease to their adult relatives. More exact details come from the following communications of more recent times:

1. Epidemic of Cremona, 1812 (Cerioli): Among 46 vaccinated children, 40 developed syphilis; and of the latter, 19 died. The remaining 6 remained healthy, and served for the inoculation of 100 other children, none of whom developed syphilis.

2. Epidemic of Grumello, 1841 (Tassani): Among 64 vaccinated children, 46 developed syphilis, and subsequently these infected several mothers and wet-nurses. There were, altogether, 10 deaths—8 children and 2 adults.

3. Epidemic of Coblentz, 1849 (Wegeler): From one apparently healthy boy, who shortly afterward developed a suspicious eruption on the nates and the inner surface of the thigh, and who died twenty days later of "water on the brain," 42 to 44 persons were revaccinated. In 19 of these (between the ages of eleven and forty) the vaccination scar broke down after four weeks and became converted into a syphilitic ulcer, following which came the symptoms of secondary syphilis.

4. Epidemic of Freienfels (Oberfranken, Bavaria), 1852: Of 13 children vaccinated at the same time, 8 became syphilitic; and from the latter, 9 others (relatives) were infected. This epidemic is of especial significance in the history of vaccination syphilis, since it led to the *cause celèbre* of Hübner, in which the physician was condemned.

5. Epidemic of Lupara, 1856 (Marone): 34 children infected from the same source, and from these other adults—in all, about 80 infected.

6. Epidemic of Rivalta, 1861 (Pacchiotti): Among 64 vaccinated children, 45 were infected with syphilis; moreover, through the medium of these latter, numerous relatives and a few wet-nurses. Altogether, 78 were infected. Seven children died. The origin of this whole group, the child G. Chiabrera, was previously suckled by a woman notoriously syphilitic, and showed a short time after its own vaccination evident symptoms of syphilis. From him alone 47 other children were vaccinated, 38 of whom developed syphilis. One of these 38 children, L. Manzoni, before he showed the symptoms of syphilis, was used to vaccinate 17 other children, of whom 7 developed syphilis.

7. Epidemic from the French department Morbihan, in Brittany, 1866 (Depaul): Over 100 children, some directly, others indirectly, infected in two succeeding generations by the same lymph sent from the prefecture

at Vannes. This great epidemic induced Depaul to actively assert the existence of vaccination syphilis, in opposition to the then general opinion of his French colleagues.

8. Epidemic of Schleinitz and St. Veit in Steiermark, 1870 (Kocevar): From material brought from Vienna, 36 children in Schleinitz and 4 in St. Veit were vaccinated. The inoculation failed to take in 3 children in Schleinitz, and in 2 in St. Veit. These five likewise manifested no symptoms of syphilis. All the other 35 developed subsequently syphilis, and several of these communicated the disease to relatives.

9. Epidemic of the Hospital of Dey, Algiers, 1880 (Layet, *l. c.*, p. 74): 58 zouaves were vaccinated from the two-months-old child of a Spanish woman. In all cases a chancre developed at the site of inoculation, and later secondary syphilis.

10. Epidemic of Turin, 1885 (Layet): 35 children were vaccinated from an eleven-months-old child. There was first the regular course of vaccinia, followed by induration at the site of inoculation, and later general syphilis.

These observations show that repeated epidemics of syphilis have occurred in the recently vaccinated, which can be referred with almost mathematic certainty to a common etiologic factor. This factor is evidently the preceding inoculation, which is therefore made responsible for the subsequent syphilis. That this presumption is not extravagant may be seen from another important circumstance, namely, that the first signs of the syphilis occurred about three to five weeks after the vaccination. This proves that the time of the syphilitic infection must have been approximately that of the vaccination.

Finally, if the site and form of the primary lesion of syphilis are considered, every possible doubt as to its causal connection with the preceding vaccination disappears. The manner of the outbreak of the syphilis was regularly such that after an interval of several weeks there appeared at the site of vaccination, originating in the remains of the vaccinia (or its cicatrix), a typical syphilitic induration, which was later, after the proper time, followed by symptoms of secondary syphilis in other parts of the body. It is therefore clear that the site of vaccination was also the site at which the syphilitic virus was inoculated into the body, and from which it had become effective.

All this was sufficient to prove the existence of vaccination syphilis without any direct experiment, yet recently such has been made, and, contrary to the earlier experiments, with positive results. In 1882 Dr. Cory effectually infected himself with syphilis from the clear contents of a vaccine vesicle of a syphilitic child. The question as to the existence of a *syphilis per vaccinationem* is therefore definitely settled in the affirmative.

Although it is now determined that syphilis may be transferred

by vaccination, it must be added that not every syphilis appearing after vaccination is vaccination syphilis. (Compare above.) Since the first vaccination usually falls in the first year of life, in which, too, the first signs of a hereditary syphilis are frequently found, and since syphilis may be readily acquired at any age, it may happen that soon after a vaccination in children or adults the symptoms of syphilis may appear without the preceding vaccination being at all responsible for it. The criterion of vaccination syphilis lies in the fact already mentioned, that after a proper interval single or multiple primary lesions of syphilis—that is, indurations—form at the site of vaccination. And it is indifferent whether the vaccination "took" or not (Hutchinson). But when this criterion is wanting—when the primary lesion does not appear at the site of vaccination, but when secondary symptoms show themselves soon after on the body, or the primary lesion is seen elsewhere, the idea of vaccination syphilis may be naturally dismissed, and with good reason.

The certainty of our criterion is somewhat lessened by the fact that the first signs of a hitherto latent hereditary syphilis or of a newly acquired syphilis may show themselves soon after a vaccination exactly on its site. That this does not lie altogether outside the limits of possibility, certain warning experiences have indicated; for it is well known that latent syphilis sometimes becomes manifest at the site of an accidental skin affection and specifically changes it. In like manner an outbreak of latent syphilis at the vaccination site is readily conceivable. Yet this is true of only the cutaneous form of secondary syphilis, and not of the primary induration. Especial emphasis is therefore to be laid on the indurated character of the specific lesion in the positive diagnosis of vaccination syphilis.

Further questions closely related to vaccination syphilis occur in relation to its origin or pathogenesis:

Two possibilities must be taken into consideration. Since in the operation two things are necessary, namely, the vaccine material (lymph, etc.) and the instrument (lancet, etc.), either may be the means of conveying the syphilitic virus. Ordinarily and in the stricter sense (compare above) by vaccination syphilis we understand only that form which has been conveyed by the vaccine material taken from an infected source; and undoubtedly the great majority of cases of syphilis vaccinata arise by this means and no other. Yet the other origin of the disease has sometimes occurred—namely, the vaccine material has been harmless, but the instrument has been

unclean; that is, contaminated with syphilitic virus. The following observation affords a striking example of this:

In a village near Lahr (Baden) in 1863 a number of children were infected with syphilis, by being vaccinated, not from an infected child, but with a lancet contaminated with syphilitic virus (Kussmaul, *l. c.*, p. 99). The child from whom the vaccine material was taken, as well as its parents, at no time, either before or after, manifested symptoms of syphilis, while the lancet had been used to open an abscess on a syphilitic patient and had not been cleaned.

With reason, therefore, Bäumler draws attention to the fact that a healthy child from whom the vaccine is taken (or vaccinifer) may be infected with syphilis by an unclean instrument, either by the lymph from him having been taken by a previously contaminated lancet, or by his opened vaccine vesicle having been infected with syphilitic virus by subsequent contact with the lancet used to vaccinate a syphilitic subject. An authentic case of such infection has not, however, to my knowledge, been so far described.

The reverse, as before remarked, is the usual way in which syphilis vaccinata occurs; that is, the infection of the person vaccinated by vaccine material coming from a syphilitic. We have already insisted on the fact that such vaccine material may appear quite normal—in fact, a perfectly normal appearance is the rule; and that the lymph of such a vaccine vesicle can be differentiated in no way from any other lymph.

Moreover, in a case of latent or not fully developed syphilis there may be no suspicious traces of the disease in the person from whom the vaccine material is taken. Yet, in spite of this, the vaccine material may convey syphilis, as experience has unfortunately taught. On the other hand, however, there is, under such circumstances, only the possibility of infection, not a self-evident necessity for such to occur. For if this were so, many who were unconsciously or intentionally vaccinated from such sources would have been infected who fortunately were not (compare above). Therefore vaccination syphilis from suspicious vaccine must be associated with special conditions.

That syphilis does not necessarily arise in the case of the vaccine being taken from a syphilitic source is proved by many experiences, but especially by the numerous negative cases reported by Joukoffsky in the St. Petersburg Foundling Home (1865–67). From 11 children with undoubted hereditary (though at the time latent) syphilis, all of whom later manifested evident signs of disease, 57 healthy children were vaccinated. The vaccination " took" in all cases, but in none was there at any time any manifestion of syphilis.

The problem as to the special conditions necessary for the transference of syphilis by vaccine matter from a syphilitic source is a theme of active medical discussion; yet so far, unfortunately, no definite conclusion has been reached.

Two hypotheses have been offered, yet neither, we may at once say, satisfactorily explains the occurrence or lifts the veil from the mystery. For a long time the opinion of Viennois, "the so-called blood theory," obtained the most credence, till it was proved insufficient. The following is a statement of this blood theory:

Viennois, a hospital physician at Lyons, in 1860 broached the opinion that a transference of syphilis by the vaccine matter of a syphilitic could take place only when, with the lymph, blood was also transferred. But if the lymph used for vaccination was clear, that is, free from blood, syphilis would not result, even when the lymph came from a syphilitic. This hypothesis was based on the indubitable fact that the blood, even in the latent stage of syphilis, carries the virus, or at least may carry it, and that therefore a noticeable contamination of the vaccine lymph with blood introduces a factor into the reckoning that must not be treated with indifference in a case where the inoculation is made from a person with syphilis. Moreover, isolated cases seem to support this theory.

In Cherbourg, in 1858, a large number of marines were revaccinated. The vaccine matter was taken from an apparently healthy soldier, who later showed that he was syphilitic. Of those vaccinated, only two became syphilitic. These two soldiers were the last of a series vaccinated, and in their vaccination, the last remains of vaccine being taken, the lymph in the lancet was remarked to be evidently stained with blood (Lecocq).

Another example is the following: In 1864, at Béziers, Sebastien vaccinated two children on the same day from the same source. The vaccination of one was done without accident, but in the second case, as the lymph was being taken, the child made a violent movement of the arm, with the result that the lancet penetrated deeply and a drop of blood was mixed with the lymph. With the bloody lymph the second child was vaccinated. The child from whom the matter was taken seemed healthy at the time, yet it had hereditary syphilis (from a syphilitic father), and showed shortly afterward a papular syphilide over the whole body. The first of the two children, who was vaccinated with the clear lymph, manifested no symptoms of syphilis; the second, vaccinated with the lymph mixed with blood, showed after twenty-two days a commencing induration at the site of vaccination, and two months later general syphilis. Moreover, in the vaccination catastrophe of Rivalta (see page 253) the blood seems to have played an undoubted rôle, for in taking the lymph from the syphilitic, G. Chiabrera, blood was remarked on the lancet.

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To these observations, in which a mixture of blood occurred with the lymph, and in which syphilis resulted, may be added a number in which it was expressly noticed that the lymph was clear without syphilis following.

Without going too much into detail, there is the large series of carefully controlled cases of Joukoffsky. It is obvious that all these observations fall in with Viennois' hypothesis, just as that author expressed it. And although it was later proved by the microscope that even the clearest lymph constantly contains some red blood-corpuscles,—that is, always traces of blood,—the difference might readily be referred to quantitative variations in the agent (blood).

Opposed to this whole argument stands the fact that over and over again lymph mixed with blood from syphilitic subjects has been employed intentionally in vaccinating non-syphilitics, without syphilis occurring in the latter.

Thus, for instance, in the 5 cases of W. Boeck, syphilis did not follow the vaccination, although the lymph was markedly bloody and the subject from whom it was taken undoubtedly syphilitic (Rahmer).

Reiter, again, expressly assures us that he has often intentionally revaccinated from syphilitics, and sometimes with bloody lymph, without the transference of syphilis.

And, finally, others (Bousquet, Taupin, Cullerier, Friedinger) have vaccinated promiscuously, without attention to the origin of the vaccine material, with lymph that was clear or bloody indifferently, thousands of people without ever seeing a case of vaccination syphilis. Under these circumstances, it is impossible to say that if the lymph is mixed with blood and the subject is syphilitic, syphilis will necessarily result in the vaccinated. Therefore Viennois' theory manifestly loses somewhat of its incontrovertible value.

Moreover, there are not wanting instances where the vaccination was done with absolutely clear lymph, macroscopically, from a syphilitic source and yet genuine syphilis vaccinata followed. In respect to this, we may mention especially the well-known vaccination experiment of Dr. Cory on himself (see above), done with perfectly clear lymph. From the experiment it is evident that the quality of "clearness" in the lymph from a syphilitic source is not sufficient to guarantee its innocuousness in every case. Therefore it also follows that Viennois' theory, considered negatively, is not sufficient to explain the pathogenesis of vaccination syphilis.

Is, then, the idea at the base of the "blood theory" absolutely disproved, and, as many assert, to be simply discarded? I believe not, and offer the following for consideration:

1. If it is determined that the blood of a syphilitic may be the medium of the syphilitic virus, which no one denies, such a blood may in any case, when mixed in appreciable amounts with the lymph, convey by itself the contagion. (Observations of Lecocq and Sebastien.)

2. Since the blood of a syphilitic does not necessarily contain, at all times, the virus in an easily contagious form or amount, as is proved by the various negative experiments with the pure blood of syphilitics, it is evident that "bloody" vaccinations do not necessarily result in vaccination syphilis. (Observations of Reiter, Boeck, and others.)

3. Since the so-called "clear" lymph, although it contains traces of blood, has sometimes conveyed syphilis (Cory's case), sometimes not (Joukoffsky's and others' cases), there is here a "*non liquet*" ["it is not clear"] that disproves the correctness of Viennois' hypothesis for the cases under 1 and 2.

4. Since syphilis may be, and apparently often is, transferred by the so-called "clear" lymph, this shows that besides the mixture of blood in appreciable amounts with the lymph, there are other factors which may be the means of conveying syphilis.

Another hypothesis in explanation of these confusing facts was formulated by Köbner. He endeavored to reconcile the contradictions by supposing a specific syphilitic lesion at the base of the vaccination papule, in syphilitic individuals, on the active secretion of which, or its passive participation in the vaccine matter (by contact or laceration of the base with a lancet), depended whether vaccination syphilis would, or would not, occur in the person vaccinated. But it is to be regretted that from the formulation of this theory until the present time no anatomic support has been found for the existence of such a specific lesion.

On the contrary, the course of vaccinia in syphilitics, usually entirely normal, declares rather against the existence of such a lesion at the base of the pock, which should be recognizable to inspection or palpation. With all respect to the investigator, therefore, I am willing to allow only a platonic interest to Köbner's hypothesis.

Consequently, the question still remains an open one, as we have previously remarked; and it is not to be desired that its solution in the future should result from experiments on human individuals.

According to the statistics of Lotz, in 1880, the entire number of cases of vaccination syphilis amounted to about 500, arising from 50 different sources. Since then a new series of cases has been added by L. Pfeiffer, so that now the number appears to be about 700 to 750. The greatest number (more than one-half) of these occurred in Italy, the classic land of vaccination syphilis, and following it succes-

sively come France, Germany, and England, and, finally (with only a few cases), Scotland, Denmark, Switzerland, and North America.

If this number at first sight shocks a few timid souls, on consideration, it must appear absolutely insignificant in comparison with the thousands of millions who in the past century have enjoyed without injury to their health the blessing of vaccination. There is likewise no ground for fear that the future will look on it more dubiously; on the contrary, the opinion is well founded that by attention to proper precautions the frightful phantom of syphilis vaccinata will entirely disappear. This is for the encouragement of the friends of vaccination, and for its enemies it is surely high time to let rest a hobby by the riding of which no more honor is to be gained.

In concluding this discussion of the pathogenesis and occurrence of vaccination syphilis one other consideration should not be omitted, viz., the possibility of a transference of syphilis vaccinata as syphilis vaccinata in the second generation.

In different reports on the epidemic occurrence of vaccination syphilis it is to be noticed that patients who had been vaccinated from apparently healthy persons, but who were in reality suffering from syphilis, and who themselves were employed as a source of vaccine matter after the maturity of their vaccinia (therefore after about a week), repeatedly transferred typical vaccination syphilis to the second generation.

This fact is absolutely substantiated, yet it is not in consequence less interesting.   In the first place, it is to be said that such a vaccination syphilis in the second generation occurs only when the subject of the first generation (the source of vaccine matter for the second generation) has himself been infected with syphilis, and later at the proper time manifests it, but never when he is not infected.   This is not to be wondered at.

Further, even when the first generation is infected with syphilis, vaccination syphilis does not regularly occur in the second, but, on the contrary, it more frequently does not occur at all.   This, too, is not strange, since even a constitutional syphilis (hereditary or acquired some time before), as is well known, is not always transferred by vaccination.   Yet the real point lies more in the fact that a subject of the first generation has hardly received the germ of syphilis and a sufficient time has hardly elapsed for the development of the primary lesion before he often shows the power of transferring the germ to others, especially by means of vaccination.

This can be referred in these cases only to the rapid proliferation

of the germ, especially in vaccinia. Whether vaccinia acts as a special irritant in this regard, or whether, as Köbner thinks, the hypothetic syphilitic lesion at the base of the papule (compare above) develops early in these cases, cannot yet be answered. Nevertheless, as a singular fact, it deserved mention here.

As to the course of vaccination syphilis, there is scarcely anything to be added. The stage of incubation is usually filled up by the progress of the vaccinia, which most commonly runs a normal course. Only after several weeks do we see the characteristic induration appear in one or more places at the site of inoculation. The further symptoms of the disease in the first or second generation need not be described, since they differ in no way from those of syphilis in general.

The prognosis of vaccination syphilis is in general serious, since deaths have not rarely occurred. This is not strange, since the great majority of those infected were children in the first year of life, for whom, as is well known, syphilis is frequently dangerous.

The treatment of syphilis vaccinata consists, first of all, in prophylaxis. This demands, in relation to the possible sources of the disease, first, strict asepsis in the case of instruments and bandages; and, secondly, a strict control of the vaccine material. Everything necessary for the proper carrying-out of these has already been stated in the section on the Hygiene and Technique of Vaccination, to which the reader is therefore referred.

We must recall at this place the fact that syphilis is a disease peculiar to the human species, and is not transferable to cattle; therefore in the question of prophylaxis of syphilis vaccinata, animal vaccine possesses the indisputable advantage of absolute safety. If for any reason it becomes necessary to employ human vaccine, care must be taken to see, as far as possible, that the subject from whom it is taken is not affected with latent (and naturally not evident) syphilis. This can be attained only by the strictest examination of the person from whom it is taken, by careful investigation of his antecedents, of the health of his parents and surroundings as far as syphilis is concerned. Human vaccine of doubtful origin is to be avoided under all circumstances. Moreover, when human vaccine becomes a necessary choice, only the "clear" lymph should be employed.

Finally, we wish to mention a precautionary measure which was not expressly referred to in the preceding chapter, and which is most suitably interpolated here: Since the first symptoms of hereditary syphilis often appear late in the first year of life, it is consequently a good rule not to choose too young children as subjects from whom to

take the vaccine.   On the contrary, it is advisable to seek out healthy children of healthy parents, who have already passed their first year.

In reference to the specific treatment of vaccination syphilis, we refer to the treatment of syphilis generally.   The method that naturally suggests itself is the antisyphilitic (mercurial), which in the case of infantile syphilis is particularly suitable.

Among the other infectious diseases which may be transferred by vaccination, leprosy is to be mentioned.   Repeated observations have lately been made in leprosy regions showing the possibility of this (Däubler, Gairdner, Beaven-Rake, Arning, Black, Diday, and Doyons).

Moreover, since Arning has demonstrated that the lepra bacilli are found in the vaccine lymph of patients, the danger has become more apparent.   I introduce here a very instructive example in which leprosy occurred, not only in the first, but also in the second generation:

A European physician living in Trinidad vaccinated his own son with matter taken from a seemingly healthy child, though it came from a leper family, and later showed leprosy itself.   The vaccinated son of the physician served as the source of vaccine matter for another healthy child.   Both these children developed two or three years later symptoms of leprosy (Gairdner).

The prophylaxis of vaccination leprosy consists in the avoidance of human vaccine matter wherever leprosy occurs frequently and there is the slightest danger of acquiring it.

There was a time when, next to syphilis, tuberculosis was the disease most feared as a possible result of vaccination.   Nevertheless, so far no single authenticated case has been reported in which a transference of tuberculosis occurred through vaccination.   With the discovery of the tubercle bacillus by R. Koch, and with the proof that tuberculosis occurs frequently in animals in the form of "Perlsucht" (pearl disease), the question naturally assumed considerable importance as to whether the bacilli were present in the human, or especially in the animal, vaccine lymph of the tubercular.   But they were not found in either case, even when the disease was far advanced (L. Meyer, Strauss, Josserand, Acker, and Peiper).   Yet the possible danger of tuberculosis vaccinata was not yet disproved.   Therefore experiments have recently been made with the view of transferring tuberculosis by the vaccination of susceptible animals.   Inoculations of vaccine lymph from tubercular subjects into the anterior chamber of the eye of the rabbit resulted negatively (Peiper).   The same is true of Schulz's experiments on guinea-pigs with the lymph of a cow

affected with pearl disease. Accordingly, therefore, the possibility of a tuberculosis vaccinata appears at best but hypothetic.

Nevertheless, it is certainly advisable to use every precaution in this regard. Human vaccine matter from an individual in whom the suspicion of tuberculosis exists should not be taken for vaccination purposes. This applies also to the vaccine matter from the bovine race with even a suspicion of pearl disease. Since calves, in contrast to older animals, are only exceptionally affected with pearl disease, it is recommended that calf lymph be chosen as the only form of animal vaccine material. Moreover, in addition, the animal should be subsequently killed in order to make the proof certain that no tuberculosis exists. The German Vaccination Law requires the slaughter of the calf after the lymph has been obtained, and an autopsy before the material may be employed.

Scrofula does not enter into the question, since it is not so much a disease *sui generis*, as rather a diseased predisposition of some individuals to certain pathologic (simple inflammatory, hyperplastic, and specific tuberculous) processes, which may be inherited or acquired, but are not caused by a definite virus. In regard to rachitis, which is perhaps (Hagenbach-Burckhardt) a specific affection, definite observations and experiments are still wanting.

With this, everything is said that relates to all the anomalies in the course of vaccinia, its complications and sequelæ. Our reports have been gathered together from many sources, yet they (relating, as they do, to its pathology only) appear insignificant when compared with the general mass of vaccination experiences.

This goes to show that in the very large majority of cases the course of vaccinia is normal, without incident, and is followed by the desired result—namely, immunity to variola.

And this remains the principal thing to the end.

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ANTI-VACCINATION AGITATION.

Like every great and epoch-making discovery, the introduction of
vaccination by Jenner, both in his own time and afterward, met not
with sympathy and encouragement, but with antipathy and open
contradiction. In other words, there was revealed once more the
transcendental power of the twofold principle of *"νεῖκος καὶ φιλότης,"*
to which, according to Empedocles, every world-stirring event must
be submitted.

The storm that arose against vaccination was no light squall, but
a full-fledged tempest, which blew in succession from every possible
point of the compass. Although it spent its violence early, and
although a century has intervened, a complete lulling of the *animus
impetuosus* has not been accomplished. Science, as a disciple of
experience and a teacher of intellectual knowledge, endeavored with
all its power to raise its voice in favor of Jenner's principle, but its
cry was not at all sufficient to still the unruly minds of the opposition.
Moreover, the opposition took refuge in metaphysics, which an appeal
to logic or reason fails to reach.

The arguments raised by the antagonists of vaccination are mani-
fold, and have—some of them, at least—changed more or less with
time. Many theses which produced considerable effect at the begin-
ning seem to-day antiquated, and have in consequence been laid
aside. Other communications, however, have proved themselves
more viable, and exercise, even at the present time, a fascinating
influence on a host of individuals. Finally, others came into existence
in later times, and have as a consequence preserved their strength.
Therefore these arguments of the opposition consist of a conglomera-
tion of the most different elements, showing there was no unity of
system in its tactics.

To detail all the individual arguments seems to me unnecessary.
I consider it much more pertinent to consider in short a few of the
more especially striking ones. I shall omit as far as possible the
names of the agitators, since undoubtedly they lose least by such an
aposiopesis.

Vaccination experienced opposition first from a religious side,
inasmuch as some overpious souls regarded the employment of a pro-
tective means against a disease sent by God as a sin. The same
argument had been used some years earlier in regard to Franklin's
discovery against the danger of lightning, and had not lost its weight.
At the present time, not only secular buildings, but churches also, are

furnished without scruple with the hitherto disreputable lightning rods, and the desecration of God's house by such preventives is never thought of. Conformably with this changed idea of Providence, we no longer see in the exercise of vaccination a crime against God, or we see it at most in the narrowest circles of the excessively pious. And it is to be noted that this religious objection was brought forward only in isolated instances by clergymen, and was especially the singular offshoot of lay intellects. On the contrary, the clergy, especially the Protestant clergy, more commonly supported vaccination with their authority than opposed it; for more than one stout-hearted guardian of souls, as the old literature shows, saw himself moved in the first years after Jenner's discovery to recommend vaccination in a popular communication, or even in his Sunday sermon, as a work well-pleasing to God (Stricker).

Much more lasting than the religious scruple was a politico-legal argument, which has continually been used against vaccination by its opponents in connection with other invectives. This was applied directly only against compulsory vaccination, but by an oratoric circumlocution was usually made to hit vaccination itself. And even at the present this argument is persistently brought to the front whenever the question of vaccination comes up, in parliaments or elsewhere, especially whenever and wherever the position of the State toward vaccination is being discussed. There is then always a violent controversy, which grows hot over the principle of compulsion, since this is contrary to the liberty and free-will of the citizens. Vaccination and revaccination are things that concern the individual, and should remain so. The State has no power to command them, and every compulsion on the line of this sanitary though decidedly controvertible question is synonymous with an illegal oppression of the individual.

It is worthy of notice that this tender regard for the rights of the individual is, in the first place, met with in those who are known otherwise as opposers of vaccination, and who wish to see it disposed of as a sanitary measure. What they actually aim at is very clear to the unprejudiced. As a matter of fact, this argument is used to influence and attract those to whom the question of vaccination would have remained indifferent. And on every occasion it has especially influenced a great host of susceptible minds, who harbor in their breasts every known manly feeling, and who, as a consequence, look on themselves as the exclusive guardians of liberty. It is therefore intelligible that political radicalism in republics and constitutional

monarchies has more than once taken up the question as a plank in the political platform, so that a whole party would work against vaccination, and agree that compulsory vaccination should be indignantly dropped by the State. Occasionally, too, in this struggle it has been found occupying in concord the same stage with piety, with which it does not ordinarily live on the best terms of friendship, but with the desires of which in this regard it participates.

It was so, for instance, in Würtemberg in 1858, when, after the publication of the English "Blue-book," a somewhat more favorable sentiment regarding vaccination seemed to have arisen throughout Europe. Here the active opposers of vaccination, Nittinger, Betz, and others, succeeded in winning to their side the democratic party of the "Beobachters" ["observers"] (under the standard of their leader at that time, Hopf), and simultaneously the "piously inclined" of the land, and in influencing them so that a petition was sent to Parliament demanding the abrogation of compulsory vaccination—which foolish request was refused. The excitement which this caused throughout the country, and which spent its rage in the Parliament, surpassed anything heretofore seen (Stricker). The introduction of compulsory vaccination in England also was a long and difficult struggle, because, apart from sanitary scruples, the politicolegal influence had so determined public opinion against compulsion that it seemed impossible to surmount it. In Germany debates about the vaccination law (1874) occasionally took place, and again also remonstrances against compulsory vaccination and revaccination on pretended legal grounds, and later even petitions were repeatedly sent to the Reichstag asking for abrogation of the law, but so far fortunately without success.

In Switzerland the law relating to epidemics (which, besides other useful things, introduced compulsory vaccination for the whole confederacy) worked out by the commission of Swiss physicians at the bidding of the Bund or Swiss Confederation, was wrecked by the opposition of the sovereign will of the people, and not from political motives; though to any one who understands the circumstances this outcome is not surprising.

In relation to the pretended illegality of compulsory vaccination (and revaccination) we must energetically insist that, consciously or unconsciously, the opposition in their attacks proceeds from totally false premises in their conception of liberty. It must first of all be understood that personal liberty and free-will have legal limits, and must under no circumstances come into collision with the common weal, for otherwise presumed right might soon develop into actual wrong. And this would be the case with the omission of a measure which, like vaccination (and revaccination), not only gives directly to the vaccinated manifest protection against smallpox, but likewise indirectly to the whole population of a region or country a safeguard that cannot be valued too highly against the epidemic spread of the

disease. In relation to the latter point,—namely, the decrease of the danger of smallpox generally,—the legal question of the protection afforded by vaccination does not consider it a matter of prime importance whether the persons who of their own free will have remained unvaccinated, and therefore susceptible to smallpox, run the risk of acquiring it in their own proper persons, appropriately enough, and succumbing to the disease. We would like perhaps to say "*Habeant sibi!*" if such a wish was not impious and inhuman. Since every new smallpox case creates a focus for other possible cases, every one who scorns the protection of his own person through ignorance is guilty of a negligence that may eventually do the greatest injury to others.

But if, for this reason, compulsory vaccination appears a very reasonable and justifiable measure which excludes the despotism of the individual and thereby serves the public weal, there is still a second reason, which is, if possible, even more convincing. It is the humane duty of the civilized State to take care of minors and protect them from the caprice of their elders. That is to say, the State should not allow children to suffer for the sins of omission of adults, and therefore it only remains true to its principles when it strictly demands the vaccination at least of children. This is even more justifiable, since variola is, especially for children, so dangerous a disease. Or shall European civilization wink at the possibility of a return of the calamity that swept away children and left a track of intense misery, only because fathers and guardians, under the name of liberty, chose to deprive of vaccination the children and wards intrusted to their care, and thereby senselessly deliver them to the caprice of that demon? Where the practice of vaccination is not an absolute custom among the people, and unfortunately this is so nowhere up to the present, legal compulsion seems the only means for preventing a mischief that especially threatens the innocent. Moreover, it would act educationally on the masses, in that it would generally come to be recognized by them as something unalterable, and so would soon develop into a custom.

The fact is also used against compulsory vaccination, and thereby indirectly against vaccination, that actual injuries to health have resulted here and there, or even in groups, from vaccination, inasmuch as on account of the inevitable trauma occasioned by the operation, other diseases of an infectious nature, especially syphilis, have been conveyed instead of vaccinia, or simultaneously with it.

It has been shown in the preceding sections with sufficient clear-

ness in what an insignificant minority these unpleasant occurrences are found, as compared with the very large total number of vaccinations and revaccinations done. Surely no one who understands the principles of sanitation would wish to do away with vaccination, the most powerful and effective protection against the most dreadful of all diseases, on account of such rare occurrences, as long as nothing worse is proved in relation to it. Moreover, we have already described in a previous section how medical knowledge and perfect technique can avoid these possible dangers. Finally, these dangers, which the present improvement in the procedure has done away with, are the only imaginable ones that can occur to the patient from vaccination. Everything else in a sanitary way that has been hurled at vaccination by the opposition has been proved foolish on closer investigation, or is at least a conglomeration of the most rash assertions. Consequently, it would scarcely be worth while to go further into these if they had not succeeded in bringing down considerable criticism on Jenner's method, thereby so materially aiding and abetting the wrong.

For these reasons, then, a short consideration of these inanities may be in place:

In order to proceed more or less historically, we may mention as a curiosity that when opposition was first raised to vaccination there were not wanting some who dreaded a bovinizing influence on the person vaccinated. More than this, some especially enlightened individuals actually perceived to their horror, with their own eyes and ears, in certain victims (children) after inoculation of cow-pox, "unmistakable" signs of beginning bovinity (inclination to quadrupedy, to bellowing like a calf, to the development of hoofs, horns, and tails), and, on account of the further development of these monstrosities and the danger of their becoming common, they prognosticated the worst for the future of the human race.

And though it did not persist long in so coarse a form, yet the theme itself was kept up unremittingly in a somewhat less threatening fashion: Vaccination was "against nature" or was "brutal" because it entered into the life of the individual in an unwarrantable way, or brought the human organism into an unclean and disgusting contact with metabolic products of lower (animal) origin. According to the taste and aim of the adversary, sometimes one, again another, variation of the text was insisted on, though frequently a confused use of both was made simultaneously and promiscuously. If the attempt is made to separate these double threads of the web from one

another and study them apart, something like the following will be found:

Vaccination is objectionable, so with emphasis and alacrity said one party (Vergé de l'Isle, Ancelon, and others), for the reason that it is an artificial and unhealthful interference with a life process that is natural and beneficial to the individual. These fanatics and their disciples regarded as a benefit of nature—we may well be astonished —variola humana, which previously almost every one had to pass through, at least once, in order to be freed from the congenital "acrimony of their humors" ("Schärfe ihrer Säfte").

With this principle the old and dead doctrine of Rhazes (compare p. 15) was exhumed and circulated once more, to a certain extent, as adopted grandmother among the living of the nineteenth century, shocking the aftercoming race with gloomy forebodings for the future; for these modern exponents of this doctrine could not do otherwise than cry "murder" at vaccination and revaccination, because both procedures were, unfortunately, for the express purpose of preventing that condition which acted as a purifying purgatory, and had succeeded in their aim beyond expectation. The cheap victim of innumerable hecatombs was not taken by them into consideration, and it seemed to them "more natural" to put variolation again in action, because this at least set in motion a proper variola, even if not always at a time suitable to the individual, which by the purification of the "humors" worked to a certain extent "critically"; while vaccination or revaccination, led by "internal necessity" to an auto-intoxication (in the present sense of the term) with the inborn acrimony of the humors, and thereby to a deplorable condition of the human being, the highly suspicious signs of which are already becoming evident.

Moreover, there was, in contrast to this edifying harmony, another that to a certain extent made a counterpoint accompaniment, and at least considerably increased the complete effect for the listeners to the concert. This amounted to the same thing as that vaccination (and revaccination also) was unnatural and detestable, and the harmful results were evident in the disgraceful renewing of it, though the nature of the unnatural and the grounds for its harmfulness were assumed almost entirely from the heterogeneity of the vaccine. If the vaccine comes once from an animal, it never becomes adapted to man, for, to say nothing more, it must act, if not brutalizingly, at least corruptingly or poisonously. Both these theories, persistently repeated, were not sharply differentiated from each other by rabid anti-vaccination prophets (Nittinger, Betz, and others), and still less

so by the masses, although in their foundation they are diametrically opposed. They instilled rather into the minds of the people a confused conception of " vaccine-poisoning," from which every one might choose what was agreeable to him.

By this wonderful, and at the same time dreadful, *mixtum compositum* the greatest mischief was done by orators and writers, especially about the middle of the nineteenth century. The principal seat of the anti-vaccination agitation was, at that time, South Germany (and in that region, thanks to Nittinger and his disciples, especially Würtemberg); yet the northern part of the present German empire, France (Vergé de l'Isle and others), England, Switzerland, and other countries contributed no mean contingent. It was impossible for many otherwise intelligent but impressionable people of all classes and callings not to be disturbed and confused by the dreadful pictures presented to them, and not to feel urged on to raise their voices against vaccination and compulsory vaccination. And when one asks if the question is not now dead, we must regretfully answer in the negative. For even though in some measure dead, the old specters still haunt us and constitute the ground on which many continue to grow unnecessarily warm over the stringent carrying-out of vaccination and revaccination.

That there is no reason for apprehension is readily shown. For if we look at the specter of vaccine-poisoning in clear light, it shrinks away to an empty nothing. The pretended symptoms of this intoxication may be said to be the following:

An evident profound (intellectual as well as physical) degeneration of the race among the civilized nations of Europe has developed during the nineteenth century as an effect of the general practice of Jenner's discovery, which is much worse than the purely external harm done formerly by variola. This degeneration shows itself in a marked decrease of intellectual power and an increasing imbecility, as likewise in a lessened power of resistance, which has brought about more unfavorable conditions of general mortality. Finally, scrofula, rachitis, consumption, typhoid fever, and other diseases, which are especially inclined to undermine the constitution and demand death sacrifices, are decidedly more frequent than formerly. Omitting the fact that these descriptions of the conditions in the nineteenth century have been made so striking in order to outbid the deleterious influence of variola in former times, it is still questionable whether, and in how far, vaccination is responsible for them, for every substantial proof is lacking which would show that they arose either singly or altogether

on account of vaccination; and, on the contrary, as soon as we come to investigate a little more closely the actual conditions, and compare them with those of earlier times, the advantage is seen at once to lie with the present age.

First, as to the intellectual power of the vaccination age and that of its representatives, we may boldly assert that the tree still bears fruit, and that the human society of Europe in the nineteenth century, even though we may complain bitterly of certain psychic excrescences, is further removed from pandemic stupidity than ever before.. To say more on this subject would be truly " carrying owls to Athens " [or " coals to Newcastle"].

Similarly favorable results are seen when we consider the physical conditions, and in connection therewith the death-rate, of the present and the past.

The general death-rate statistics since the introduction of vaccination are not only not more unfavorable, but decidedly improved. Since these are the truest reflectors of the physical powers of a generation, it follows that a physical degeneration of the race is not to be thought of.   Where these relations are properly and accurately traced among large masses of people and over long intervals, we are able to determine absolutely that a decrease in the death-rate *pro rata* (or the mortality) and a lengthening of the average and probable duration of life have taken place, without any compensation for the deaths caused previously by variola.

Therefore all the antagonistic assertions of the anti-vaccination agitators mentioned and enumerated above must be pronounced false.   This is seen more evidently from the following facts:

The death-rate statistics of the kingdom of Sweden show that (compare English "Blue-book"), in the years from 1756 to 1775, the yearly death-rate was 28.9 per 1000 inhabitants; in the years 1776 to 1795, 26.8; while it was in 1821 to 1840, only 23.3; and in 1841 to 1850, only 20.5.   The general mortality, therefore, during the nineteenth century in Sweden has sunk almost one-third, and this decrease did not cease or make way for an increase when, in the mean time, vaccination became general throughout the country.

In London (according to Greenhow) the annual death-rate per 1000 in the years 1681–1690 was 42; in 1746–1765, 35; while in 1846–1855 it was only 20, or, in comparison with the end of the seventeenth century, not more than half.   The average duration of life in Europe in the seventeenth century was approximately only about thirteen years; in the eighteenth, twenty years; while in the nineteenth century it increased rapidly to almost three times the first figures—namely, thirty-eight years. The expectation of life has likewise evidently become greater in the nineteenth century.   So, for instance, in Geneva (according to Marc d'Espine)

the probability of reaching the tenth year among 100 children born living during the interval from 1701 to 1760 was only 60%, while from 1814 to 1833 it was 73%; further, the probability of reaching the fortieth year among 100 who were ten years old in the first interval was 68%, in the second, 72%; the probability of reaching the sixtieth year among 100 who were forty years old in the first period was 59%, in the second, 63%.

It is scarcely necessary to mention that this improvement in the general mortality and the prolongation of the (average and probable) duration of life is by no means due alone to the introduction of vaccination, yet this was not the question. This favorable change is due much more to the general improvement in the hygienic conditions which went hand in hand with the advance in culture throughout Europe. The only question we had to prove, and which the previous statistics do demonstrate, was the contradiction of the senseless assertions of hot-headed anti-vaccinationists, that vaccination had exercised an unfavorable influence on the general mortality and on the average and probable duration of life.

Moreover, just as no increase manifested itself, so likewise there was no unfavorable displacement of the mortality after the introduction of vaccination, as the anti-vaccinationists boldly affirmed.

H. Carnot (artillery officer at Autun), in 1849, developed this doctrine in a much quoted paper, and some years later (1851), in a second publication, endeavored to establish it more firmly. According to him, as a result of vaccination and the decrease in the number of deaths in early childhood induced by it, there has occurred a "déplacement de la mortalité," in that, instead of the general death-rate falling as formerly in the non-productive age, it takes place now unfortunately in the productive ages between fifteen and forty. And this signifies inevitably from the standpoint of national economy the coming "ruin of human society."

The statistics on which Carnot based his theory imposed on many who are accustomed to look on figures as figures, without inquiring how they were obtained or what might be the result if they were used in a contrary sense. Others more far-sighted looked with suspicion on Carnot's results, and Dupin, Bertillon, and others undertook the perhaps superfluous, yet serviceable, task of demonstrating the fallacies in Carnot's method and of placing them in the pillory of public opinion, as they deserved, as contrary to the fundamental conceptions of scientific statistics. Therefore it is unnecessary to repeat here in exact figures the reversed account of his fallacious estimations at their true worth. Yet it is perhaps not entirely out of the way to show, by way of contradiction, namely, that the natural time of death for those living in the nineteenth century (therefore, since the introduction of vaccination) has been put off, not only in

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general (that is, for all ages taken together), but particularly for the "productive" period of life (that is, for the ages between fifteen and forty). In this we will positively prove the reverse of what Carnot asserted—namely, that the conditions of life have grown more favorable for the productive age.

The annual death-rate in Sweden per 1000 for the different ages was as follows:

					1776 to 1795.	1841 to 1850.
Between	0 and	5 years		....	85.0	56.9
"	5 "	10	"	....	13.6	7.8
"	10 "	15	"	....	6.2	4.4
"	15 "	20	"	....	7.0	4.8
"	20 "	30	"	....	8.9	6.8
"	30 "	40	"	....	11.6	9.8, etc.

N. B.—This same decrease in the death-rate is seen in Sweden in all ages up to 100 years. It is therefore general.

The annual death-rate in France (according to Bertillon) in the especially interesting "productive" period per 1000 was:

					Middle of the eighteenth century.
Between 20 and 30 years				....	14.7
"	30 "	40	"	....	21.5
		against:			1849 to 1859.
"	20 and 30 years only			....	10.7
"	30 "	40 "	"	....	9.7, etc.

N. B.—In France, too, this decrease in the death-rate may be followed through all ages.

These figures, to which others of a like kind could be added, teach plainly the untenableness of Carnot's displacement theory. The principal error of this lay simply in the following: Carnot proceeded exclusively from the mortality conditions of the capital of France (Paris), not realizing that this might not represent the proportionate statistics of the whole country. Besides this, he took into consideration merely the absolute mortality, not the mortality at the different ages, not realizing, again, that the productive age in Paris (as in all large cities and centers) is out of all proportion to other ages, and therefore must naturally participate in disproportionate numbers in the general mortality of the city. It is owing to the two previously mentioned French writers that Carnot's statistics were rectified, and that it was shown that the mortality of the "productive" age in Paris was not to be wondered at (omitting that of the rest of France, see above).

As to the presumed increase in the morbidity and mortality of rachitis, scrofula, and phthisis, further, of typhoid fever and other acute infectious diseases, there is no more or less to be said than that these assertions (that all other affections have become more frequent and more fatal on account of vaccination) are without foundation. It is surely impossible to speak of a compensation of the earlier death-rate from variola by means of the deaths from these and other dis-

eases, for then the general mortality in the nineteenth century would not have decreased, nor would the average and probable duration of life have lengthened (see above). Moreover, that rachitis and scrofula have become more frequent in children since the introduction of vaccination has not at all been proved, while it is certain that previously both were very frequent, and that aggravated forms of both, on account of the lack of proper hygienic measures and suitable nursing, played a particularly prominent rôle in the morbidity and mortality of childhood. Again, it is absolutely false that these two diseases are at present more frequent in vaccinated than in unvaccinated children; for a study of a very large number of cases has shown just the opposite (Löschner). As to pulmonary consumption, it still remains the most common cause of death, as in prevaccination times, for although about 1 in every 10 deaths was previously ascribed to variola, phthisis surpassed it. Yet at present, though it counts its victims in numbers, it does so without distinction—that is, without predilection for the vaccinated or the non-vaccinated, as the comparative statistics of all the countries of Europe show.

Finally, that typhoid fever and other acute infectious diseases should have gained an absolute ascendency as a result of vaccination is contradicted by any intelligent reflection, for the causes and spread of these diseases stand in no imaginable relation to vaccination.

Summing up, then, all that has been said, it is evident that nothing positive can be assumed in relation to the injurious influence of vaccination on the health of our day, either generally or in particular, and that thereby the "post hoc" doctrine in regard to the "poisoning of the masses" by vaccination is deprived of every actual and hypothetic support. This doctrine, moreover, is shown to be one of the saddest aberrations of the human reason, or perhaps it may be more properly described as a crime against the most beneficial discovery in prophylactic medicine ever made hitherto.

What still remains of the efforts of the anti-vaccinationists is little, and yet it is something, for this Pandora's box seems almost inexhaustible. As the arguments in regard to the general dangers of vaccination fell to the ground, other means were found to discredit its protective power. Among these may be mentioned, first, the assertion that the decrease in variola mortality in the first decade of the nineteenth century was not the result of vaccination, but of a natural abatement in the disease. How false this conclusion is, has been shown previously. (Compare pp. 225 and 235.) To this class of arguments belongs, further, the earlier dished and now recently rehashed fact

that the occurrence of numerous wide-spread and virulent variola epidemics in the nineteenth century, especially the pandemic of 1870–1873, proves clearly that the protection afforded by vaccination does not extend far. To this we reply that it is exactly those epidemics and this pandemic that taught irrefutably the great difference in susceptibility and in the death-rate between the vaccinated, the revaccinated, and the non-vaccinated (compare pp. 231 and 236). Finally, the absolutely unsuccessful attempts, by means of the grossest inaccuracies in the adaptation of the statistical material (A. Vogt, Böing, Lorinser, Reitz, Hermann), or by the evident falsification of them (Keller), in order to prove that vaccination was useless, or even injurious, are best treated with silence, especially as these adversaries have already been thoroughly refuted by Lotz, L. Voigt, Körösy, and others.

The hazardous undertaking of giving in the preceding statements a summary of the anti-vaccination agitation, and of analyzing the motives of its defenders, may have entirely or only partly succeeded, yet so much must be clear, that the whole movement contains in itself something perplexing to a thinking and reflecting common sense (compare the remark at the beginning of this section). The further prognosis of this movement is self-evident, namely, that, in my opinion at least, the subject is not yet fully exhausted. Nevertheless there is no doubt as to the final conquest of the right, inasmuch as the power of good is greater than that of wrong.

Whether in place of vaccination a still better protective means will be found in the future against variola, or whether the opposition will gradually lose in strength, so that it will be unable to continue the struggle, the anti-vaccination agitation in its present form will inevitably die in time. In order to hasten this necrobiotic process, the friends of vaccination must continue to use all their powers of persuasion and reason.

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CLOSING REMARKS.

At the close of this treatise on Vaccination (and Variola) the author believes he still owes the reader a résumé of the whole question, which may be put as follows:

Up to Jenner's time, and the inauguration of vaccination by him, variola was the most common and most deadly of all epidemic diseases. No remedy was of use against it, no protective means had been found to banish the dread associated with its name. Moreover, inoculation had not fulfilled the expectations with which its friends had greeted it, since all sorts of defects, and especially a certain amount of danger, were ineradicably connected with it. Vaccination was the first means that produced a change in a prophylactic respect, and thus Jenner's decided advance and its immediate consequences proved a deliverer in fact.

Again, vaccination fulfils the claims of a perfect prophylactic against variola. It is easily performed and its practice is dangerous to no one. It lends to the vaccinated, when it takes, an almost sure temporary protection against smallpox. Actual injuries to health in general are not to be apprehended, and the doctrine of the degenerating influence on the race is simply false.

A transference of other contagions (erysipelas, syphilis, etc.) by the act of vaccination has happened, and may happen; yet these accidents can be almost absolutely avoided by the use of vaccine material from a known source, and by its inoculation under aseptic precautions. Substantial objections cannot therefore be raised

against vaccination on this account, even leaving out of count the fact that these accidents are, on the whole, very rare. The diminution in the morbidity and mortality of variola in the nineteenth century is the result of vaccination and of nothing else. The natural contagiousness and malignancy of variola have not grown less, for the non-vaccinated are attacked when the opportunity occurs even as readily and succumb as frequently as in former times. If the non-vaccinated suffer less from the disease at the present day, this is due to the fact that epidemics are now less frequent and less extensive, as a result of vaccination, and accordingly the opportunities for infection are less common.

The immunity acquired by vaccination is, as a rule, not lasting. The susceptibility recurs after a certain time and increases gradually till it may become as complete as previously. Therefore even the vaccinated may be later attacked by variola, and severely (with a fatal termination), if a renewal of the vaccination after the proper interval is neglected. Yet the beneficial influence of one vaccination (done in infancy) is evident in that the relative morbidity and the relative mortality for the vaccinated in a mixed population during an epidemic of smallpox is decidedly less than for the non-vaccinated.

Revaccination and its periodic repetition renew the complete temporary immunity. The successfully revaccinated are attacked proportionately the least seldom, and succumb to variola only very rarely. Revaccination and its periodic repetition are therefore—considered from a prophylactic point of view—to be regarded as an indispensable supplement to vaccination, without which the whole practice of vaccination remains only half a measure. Moreover, the success of revaccination in individual cases indicates whether and to what degree susceptibility again existed.

Scruples on the part of the State against compulsory vaccination must be designated as weak, since vaccination is not only useful to the individual, but indirectly protects the whole community. Moreover, compulsory vaccination of children is not only a desideratum, but an ethical duty, since children as yet without the power of deciding for themselves should not be given over arbitrarily to their elders and thereby eventually become the prey of variola.

Every endeavor should be used to bring about the introduction of compulsory revaccination (for the whole population). As compulsory vaccination has met with such success in reducing the general death-rate from smallpox among children to a minimum, so experience up to the present with compulsory revaccination (as seen in certain

European armies, and throughout the whole German empire) teaches us the conspicuous utility of this procedure, so that an active opposition to it ought nowhere to be raised. And when the present time thinks otherwise, as it certainly does in some places,—for the door has not even now opened everywhere to the idea of compulsory vaccination,—it demonstrates that it does not possess a mature understanding of one of the most important questions in hygiene.

In the conscious security of the body against the threatening assault of infection lies not only one of the principal problems of hygiene, but an actual problem of human culture. Should the *homo sapiens* live up to his name, and show indeed that he is the "master of creation," he will then demonstrate by prophylaxis that the spark of Prometheus was for him not snatched in vain from heaven.

VARICELLA.

BY

THEODOR VON JÜRGENSEN, M.D.

VARICELLA (CHICKEN-POX).

ETIOLOGY.

THE relation between varicella and variola is a fact of very great importance for the general public.

Is the same pathogenic cause operative in both affections, or not?

If we answer in the affirmative, then further consideration is necessary.

Can variola be carried from a varicella patient to a person susceptible to the disease?

If this is so, then varicella belongs to those epidemic diseases which must be strictly guarded against, and which are in the last degree of similar importance to smallpox.* The views are not perfectly clear. The supporters of the doctrine that the two diseases are essentially different—the dualists—have, in my opinion, the better ground for their belief. But it cannot be denied that their opponents, the unitarians, advance many ideas which should be considered.†

What is to be cleared up in the discussion of this question belongs to the realm of etiology rather than to that of symptomatology. I will call attention to the following points:

1. Inoculation of the healthy with the contents of the vesicle of varicella.

Among the chief results are the following: Variola has never followed the inoculation of fluid from the vesicle of varicella, whether those inoculated with it had had vaccinia or true smallpox, or whether they had remained unaffected by the one as by the other disease.

In most cases, no result followed the inoculation of the varicella lymph, either local—that is, limited to the place of inoculation—or

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* The same conclusion is drawn by Bohn, Gerhardt's "Handbuch der Kinderkrankheiten," Bd. II, S. 333.

† Likewise Kassowitz, "Die Unität der Variola und Varicella," "Jahrbuch für Kinderheilkunde," Neue Folge, Bd. VI, S. 160 ff.—Eibenschitz, "Die Variola-Varicellenfrage," "Eine literar-historische Studie," Ebendort, Bd. IV, S. 205 ff.

general. We must conclude, therefore, that varicella is not capable of being conveyed in this way.*

The question stood thus as regarded the older investigations, which, with a single exception, might apply in opposition to the opinion of those who undertook them. Let this remain undecided, since the sources of information are not sufficiently easy of access. But the published observations of Steiner,† the justly esteemed children's physician of Prague, are quite free from objection. He has, in all, inoculated 10 children with the varicella lymph, eight times successfully and twice without result.

Two of these experiments may be given in detail. One inoculation was in a four-year-old boy, who had been vaccinated two years before; distinct scars told that a positive result had been obtained. The second case was that of a two-year-old girl, who had never been vaccinated nor had had smallpox. After an incubation of eight days in both cases, the varicella vesicles appeared, spreading over the whole body and accompanied by the corresponding general phenomena. The point of inoculation itself showed no reaction, but dried up in a few days.

This proves that varicella as a specific disease may be conveyed directly by inoculation.

Of more importance are the negative results obtained in a long series of attempts. In all, about 30 to 40 inoculations of varicella lymph were made on those who had not been vaccinated or had the smallpox. In the nearly universal susceptibility to smallpox, it cannot be assumed that all those who were inoculated belonged to the few insusceptible ones.

2. Varicella, after recovery, does not protect from smallpox and vaccination, nor do the latter protect against varicella.

This fact is very frequently observed, and will be unreservedly admitted even by the unitarians.‡

It appears to me to have but little bearing on the main question at issue, to discuss all the different possible combinations of the diseases one by one. Of these, may be mentioned: (a) Varicella vesicles and vaccination pustules are found together. Clinical observation teaches this unequivocally. Experiment shows that in simultaneous inocula-

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* Vetter, "Ueber das Verhalten der Varicellen zu den Pocken," *Virchow's Archiv*, Bd. xxxi (1864), S. 400 ff. An older communication by the same: "Impfung von Varicellen-lymphe," *Archiv der Heilkunde*, Bd. i (1860), S. 286 ff.

† "Zur Inoculation der Varicellen," *Wiener medicinische Wochenschrift*, Jahrgang 1875, S. 304 ff.

‡ Kassowitz, a. a. O. S. 162.

tion with varicella and vaccine, the latter develops, while the former shows no results.

Kassowitz, on the other hand, says that "varicella and vaccine are not perfectly indifferent to each other." He bases this view upon two of his own observations and on one made by L. Fleischmann.*

Kassowitz in one case vaccinated a child on the 29th of December, which on the 25th had fallen sick with varicella. One week later, on the 5th of January, a very small papule appeared at each point of inoculation, and on the 9th of January (the eleventh day) the vesicles were small, about the size of a lentil, very hard to the touch, and surrounded by a narrow zone of inflammation. The lymph obtained by pricking these vesicles was perfectly clear, and produced typical vaccine pocks in the brothers of the child.

In the second case the inoculation was made on the 15th of June on a child attacked with varicella on the 14th. On the 22d of June no results had followed the inoculation, which, however, was not repeated. On the 2d of July (the seventeenth day) the mother brought the child for inspection. On the right arm appeared a pustule of the size of a finger-nail surrounded by a large area of inflammation, the contents purulent and drying in the center. The whole appearance corresponded to the normal development on the tenth day. This corresponded also with the report of the mother, who said that she had first seen the red points on the day after the child was first seen.

Fleischmann makes only the general statement that the development of the pustule is delayed for many days and the involution takes a very slow course. It seems to me that the conclusion of Kassowitz from these facts is hardly justified, all the less so as Vetter reports nothing of the kind regarding his inoculations—simultaneous vaccine and varicella inoculations. Delays in the development of the vaccine pustule are surely not so infrequent.

(b) Varicella and variola occur together and varicella occurs after variola; less frequently, if at all, is the opposite true.

Kassowitz also here raises objections against the conclusion that one form does not protect against the other. He asserts that no conclusion is to be drawn from it except the possibility of their occurring together or after each other. Now, it happens that vaccinia may show itself with variola, just as the vaccinated may afterward have variola, although the activity of each of the two stands unquestioned. In passing, it may be said that the longer period of incubation of the true smallpox may explain satisfactorily the local results of vaccination. At the time of vaccination the patient may already have in his system the poison of variola; while it remains latent, the vaccine virus, needing less time for development, exerts its influence. It is also known that under these circumstances the protection afforded by vaccination is restricted. The subsequent relation of cow-pox to smallpox is hardly to be considered here, for we know that not even one attack of smallpox itself protects every one for all time against reinfection.

*"Ueber Varicella und Varicellen-Impfungen," *Archiv für Dermatologie und Syphilis*, Bd. III (1871), S. 498 (Beobachtung 4).

3. Are there reliable observations which show that a person having varicella may give true variola to others? This is the essential point, and if the question can be answered in the affirmative, the identity of the two diseases may be considered as proved.

It is unusually difficult to obtain reliable facts on this point. In all the older statements, made before the time of protective vaccinations, and when smallpox was widely prevalent, varicella was not strictly differentiated from the lighter cases of variola.* Where vaccination has been actually naturalized there are no opportunities for observation.

The external form of the pustule does not differ. Kassowitz † quotes the statement of Gerhardt: ‡ "that a form of disease similar to varicella arises at times from undoubted inoculation with true smallpox both in persons who have been vaccinated and in those who have not. It would be of great practical importance to be able to distinguish this varicella-like smallpox, from which true smallpox may arise by inoculation, from simple varicella. As positive indications, however, only these two points can, up to the present time, be given: The ability to produce true smallpox by inoculation and the production of true smallpox."

The case recently presented by Fürbringer § shows how impossible it may be to arrive at the correct etiologic diagnosis. Kassowitz himself advances no convincing arguments. Expressing himself in general terms, he observes with conscientious self-criticism: "It is surely permitted that one deduce individual convictions from a large number of self-made observations, and only on this account will I speak of my own experiences." ‖

Only one case is known to me which requires special consideration, the case presented by Karl Hochsinger,** of Vienna. The following is a brief description of it:

"In the month of April, 1890, Franz K., a lad aged ten years, a Gymnasium student, was attacked with varicella. Fourteen of his school-

* Compare with this: Heim, "Ueber die Diagnostik der falschen Pocken mit Hinsicht auf die neuerlich behaupteten Fälle von echten Pocken nach vorhergegangener gelungener Vaccination," *Horn's Archiv für praktische Medicin und Klinik*, Bd. VII, Heft 2, S. 183 ff.

† a. a. O. S. 171.   ‡ "Lehrbuch der Kinderkrankheiten," 4 Auflage, S. 97

§ "Die jüngsten Pockenfalle im Krankenhause Friedrichsheim," *Deutsche medicinische Wochenschrift*, 1896, S. 4 ff.

‖ a. a. O. S. 170.

** "Zur Identitätsfrage der Pocken und Varicellen," *Centralblatt für klinische Medicin*, XI. Jahrgang (1890), S. 769 ff.

mates, according to the school reports, were kept from school at the same time on account of varicella. I observed in the boy a typical case of vari-cella with a few quickly developed, clear vesicles. The affection ran its course smoothly in a few days without causing the least rise of tempera-ture or confining the child to his bed. The older brother of the boy, Hans K., aged thirteen years, a pupil of the same Gymnasium, but of a higher class, in which there was no varicella, was kept from school from the day on which his brother was attacked, on account of our sanitary laws. Without being isolated, he remained at home with his brother and his mother, a lady forty years old, who also stayed indoors to prevent spread-ing the infection.

"On the twelfth day after the outbreak of the exanthem in Franz K., his brother and mother were taken sick at the same time. The older brother presented a typical picture of varicella, but the mother had var-iola vera of a severe type." The description of the course of the disease leaves no doubt that the mother really had genuine smallpox and I will omit the details. "The vaccination history of these patients is of great interest. Both boys were vaccinated in their infancy and then again in 1885. The mother had been vaccinated three times, once in childhood, again fifteen years before, and last five years before, at the same time that the boys were vaccinated. In all the members of the family the vaccination was in each case successful."

Hochsinger draws the conclusion that "variola and varicella are etiologically identical." He, however, expresses himself altogether in opposition to the "observations" of Thomas, who considers all these cases as variola, in a brief answer to the above:* "I have in my communication been at special pains to show that the form of disease in the two boys was what we diagnosticate as varicella infantum. If, however, we classed these two cases as variola levissima, we should have to divide those forms of disease which in children appear under the form of varicella into two groups, one group of which represents non-specific, non-variolous varicella, while the other represents a very light but genuine variola of childhood. We should have to admit that we are not in a position to distinguish these two forms clinically."

Such a conclusion is perfectly justifiable, but I should not consider the explanation of these cases as satisfactory.

It is very strange that 15 students of a gymnasium class, who belong to the higher classes of society and were still under the protection of vac-cination, should at the same time have smallpox even in the lightest form, at a time when, as Hochsinger states, not a case of variola vera was reported in Vienna. On the other hand, the simultaneous occurrence of varicella among so many children who were at just the limit of the age when the susceptibility to this disease is lost † is not less strange. Add to this that the mother, who, five years before, had been successfully vaccin-

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* Both in the same place, pages 850 and 851 of the Annual in question.

ated for the third time in her life, and thus, according to all experience, was strongly protected from smallpox, was infected with the slightest form of the disease and had to undergo the severe type. I cannot explain these strange phenomena. I only believe that this observation, standing, as it does, by itself, does not apply to the question of identity.

4. With regard to the differences between variola and varicella, it is important to state that the latter is, if not wholly, yet practically, limited to the age of childhood—the first ten years of life.

That smallpox in its time did not spare these ages its stern rule is as certain as that they were not visited exclusively by the lightest form. On the contrary, the mortality of children was very materially increased by smallpox. Is it probable, then, that even in non-vaccinated children only the lightest form of variola should appear, scarcely ever causing a death? The objection that this may depend on vaccination, which has become a part of mankind and may to a certain degree protect their children, is not to be taken seriously. One need only show that in earlier times many, probably most, of the children were born of parents who had had smallpox.

What Kassowitz advances against this view is of no importance; it is the weakest of all his arguments. He deals only with the local manifestations, the vesicle-formation in varicella and the pustule-formation in variola. This difference he ascribes to the difference in the skin, its tenderness in the child. We need not dispute about this. Only the general manifestations can be decisive.

5. The epidemic relations are said to be different in variola from those in varicella.

Thomas * attaches some importance to this diagnostic point, but I believe that it is better to disclaim it. The differences show nothing so peculiar that several explanations are not possible, and this explains the difficulty of diagnosis in individual cases. .The remarks of Kassowitz would be appropriate here. If I now sum up everything together, I must place myself on the side of the dualists, and say with them: Varicella and variola are essentially different diseases.

Over the other points of etiology we can pass quickly. They deal rather with what is external and obvious.

1. The disease is usually spread from one person to another. In what way this takes place is as little known as in the acute exanthems. We have already spoken of the results of inoculation.

2. Extensive epidemics are very rare; the disease is usually

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* " Ein Beitrag zur Kenntniss der Varicellen," *Archiv für Dermatologie und Syphilis*, Bd. I, S. 352; and in v. Ziemissen's " Handbuch," Bd. II, 2, S. 9 der 2. Auflage.

endemic, but at times occurs in a greater number of cases. At such times the kindergartens, primary schools, and such places afford abundant opportunity for infection.

3. Varicella occurs throughout the whole year. Greater susceptibility at certain periods of the year has not, at least hitherto, been shown, but seems to be different in different places.

Thomas * collected for the years 1842–1868, from the reports of the Leipzig dispensary physicians, the cases observed by them and diagnosticated as varicella. There were, in all, only 435, in contrast to the 543 diagnosticated as variola. Leipzig increased considerably in population during these years, especially during the later ones. In 1868 the number of varicella patients reached 55, against 31 for the three immediately preceding years. From 1842 to 1865 the numbers vary between a minimum of 5 and a maximum of 22 cases. The smallpox cases also reached their maximum in the two maximal years of varicella (1842 and 1868). That mistakes in diagnosis have slipped in seems not to be doubted, but this cannot of course be proved.

All seasons of the year have their share of cases, but the half-year from July to December is especially burdened.

On the other hand, I might give my own Tübingen observations, which deviate considerably from the last-mentioned statement, but in the main correspond. From 1873 to 1894, 133 cases of varicella were treated in the Tübingen policlinic, and not a single case of smallpox.

The maximal years were 1880, 1881, and 1891, with 12 cases in each year. The minimal year, 1890, with no cases. The distribution in the different times of year, reported in percentages of the whole number, was as follows:

	Leipzig.		Tübingen.	
January to March	20.5	} 46.5	23.3	} 63.9
April to May	26.0		40.6	
July to September	23.7	} 53.6	13.5	} 36.1
October to December	29.9		22.6	

4. Varicella is a disease which is quite peculiar to the age of childhood. Observations all agree on that point. Most of the cases occur before the tenth year. It is unnecessary to give individual examples, since all writers say the same. Even the unitarian Kassowitz reports that he has not seen a case later than the ninth year. By most authors it is asserted that susceptibility is lost at puberty. [Thomas never saw an adult suffering from varicella (" von Ziemssen's Cyclopædia.")] Bohn,† however, reports that he observed one case

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* *Archiv für Dermatologie und Syphilis,* a. a. O. S. 353.

† "Gerhardt's Handbuch," Bd. II, S. 326.

in a sixteen-year-old girl whom he had vaccinated a month before with almost typical results.

[The statement that varicella is exclusively a disease of childhood is to be received with great reserve. Baader, of Basle, carefully noted 584 cases—382 occurred in children aged from one to five years, 191 from six to ten years, 7 from eleven to fifteen years, 2 from sixteen to twenty years, and 2 from twenty to forty years. In 1889 a friend of the editor, aged twenty-five years, himself a member of the medical profession, had in Dublin a well-marked attack of varicella. In June, 1894, a barrister aged thirty-two years passed through a typical attack under the editor's care. In the *Lancet*, May 12, 1883, H. Grabham Lys, M. D. Lond., of Bournemouth, reported that he had then recently had under his care three sisters, all adults, suffering from typical varicella. The first of these cases was not traceable to a definite source of infection, but chicken-pox was rife in the neighborhood. The other two cases arose exactly fourteen days after the onset of the first, and were no doubt contracted from the sister. On the ground that infection of adults was so rare in varicella, Lys had allowed the three sisters to associate with one another. He had previously seen a severe case in a nursemaid. In the *Lancet*, March 10, 1894, Malcolm Margrave states that he had recently attended a family in which three children had well-marked chicken-pox, the infection being conveyed by their mother, aged thirty-one, who had vesicles on her chest, back and abdomen, and face. She had contracted the disease through visiting a friend whose child was convalescent from varicella. In his most graphic and truthful description of variolæ pusillæ, or chicken-pox, William Heberden says: "I saw two children ill of the chicken-pox, whose mother chose to be with them, though she had never had this illness. Upon the eighth or ninth day after the pocks were at their height in the children, the mother fell ill of this distemper then beginning to show itself" ("Commentary on the History and Cure of Diseases," 1782). Dr. Willan, in 1806, described an undoubted case of varicella in the person of a gentleman aged thirty years, and Dr. George Gregory, Physician to the Smallpox and Vaccination Hospital, London, in the fourth edition of his " Elements of the Theory and Practice of Medicine" (1835), states that "in one instance, at the Smallpox Hospital, I observed the disease, in a very genuine form, attacking an adult female."]

5. Varicella may occur repeatedly in the same person. Gerhardt * says: "The protection secured by one attack is more uncertain than

* "Lehrbuch," a. a. O. S. 97.

in smallpox; I have treated one child three times for varicella." He does not make a detailed report. [As a rule, chicken-pox does not recur, though Trousseau says that second attacks are not uncommon.]

6. Duration of the stage of incubation: In the inoculations of Steiner which were accompanied by results, the period of incubation was eight days. For the usual method of infection, the average period of incubation is about thirteen or fourteen days, with a maximum of nineteen days, but accurate observations are wanting.

PATHOLOGY.

GENERAL DESCRIPTION OF THE DISEASE.

No noteworthy symptoms usually precede the outbreak of the eruption. This appears quickly, spreading from above downward. We first see rose-red, slightly raised points, from the size of a pinhead to that of a lentil, rarely as large as a silver 20-penny piece. They are in many places so closely crowded that they run together. The further development varies; a few heal without further development, but most of them become vesicular. The vesicle begins in the middle of the red spot or macule and spreads rapidly, so that in a few hours, at the most in one day, they have reached their full maturity. At this time they are covered with a thin, transparent, tightly stretched membrane and filled with a clear or slightly cloudy yellowish fluid. Only exceptionally are they multiple. If we prick them, an albuminous, neutral or weakly alkaline fluid containing a few leucocytes exudes. The vesicle dries up in a short time, being replaced by a crust which falls off in a few days, leaving a slightly reddened or pigmented skin, which soon presents a perfectly normal appearance.

In some cases of more extensive eruption some portions are found which are distinguished from true smallpox eruption only by the shortness of the time needed for their development. Hard, circumscribed thickenings of the skin,—they might surely be called papules,—with greatly reddened and swollen areas of inflammation, purulent contents, and later permanent pitted scars. Varicella causes considerable itching, the consequences of which can generally be seen on the skin of children affected. The mucosa of the mouth, especially of the hard palate, and less frequently other mucous membranes, show vesicles and a simultaneous catarrhal affection. Any deeper changes are seen very rarely, if at all.

The temperature remains at nearly normal height in the lightest cases only.   If it had not risen before, then it begins to rise at the beginning of the eruption, and continues at a more or less high point to the end of the eruptive stage.

CONSIDERATION OF THE INDIVIDUAL SYMPTOMS.

DURATION. PRODROMES.

WE cannot divide the course of this disease into definite sections, each presenting symptoms peculiar to itself—stages.   It may rather be said that the vesicles develop independently of each other and continue to develop so long as the influence of the infection lasts.

The infection is, with very few exceptions, at an end when no new changes in the skin become visible.   In this connection such a general expression is justifiable, for vesicles do not necessarily develop from roseola spots.   Generally we may reckon on one or two weeks for the whole duration of the attack.

Thomas[*] once saw the rather numerous roseolæ disappear from the skin after about thirty-six hours, without forming vesicles. Such cases may be more frequent, but they are not observed, because people know the slight danger of varicella and ascribe no importance to vesicles which do not appear in large number.

Thomas [†] also reports that he has seen single vesicles appear a month after the beginning of the eruption. He expresses himself rather doubtfully about their relation to varicella; he says that these stragglers are often not very characteristic, and that their place in the attack of varicella is not quite free from doubt. This is a diagnostic question which would have to be settled in each individual case. If they are really varicella vesicles, then one must consider it either a single infection which is protracted so long or a reinfection.

A statement as to the time necessary for the retrogression of the vesicle can hardly be made, and is of slight importance.   It of course depends upon the degree of the development, and also upon whether some external influences—scratching, rubbing through the clothing, etc.—have irritated it or not.

The nephritis which sometimes occurs as a sequela of varicella may also be seen early on the third day.   It is usually met with in the first or second week dating from the beginning of the eruption.

[*] In v. Ziemssen's " Handbuch," a. a. O. S. 14.

[†] In v. Ziemssen's " Handbuch," a. a. O. S. 20.

Do disturbances occur in varicella before the appearance of the eruption—are there, in a word, true prodromal symptoms?

No one questions that this is possible, but some deny, while others assert, that it is the rule.

Bohn* expresses himself rather positively: "Healthy children are for half a day pale, cross, tired, and have not their usual appetite; the next night their sleep is disturbed, there is some fever, and on the next morning the spots are noticed."

Gerhardt † speaks still more decidedly: "The disease begins with a slight chill or a sudden rise of temperature. The prodromal symptoms are mild, with or without slight pains in the back and limbs, and last often three days or more, but usually only one-half to one day."

Henoch ‡ thus asserts the contrary: "The exanthem usually appears without prodromal symptoms. Only twice has complaint been made of pain in the head, vomiting, and fever before the appearance of the eruption. Now and then a conjunctivitis or a sore throat is met with, which I regard as accidental rather than as directly connected with varicella."

Thomas ₰ shows again the propensity peculiar to Wunderlich's pupils to draw a dividing-line between "normal" and "anomalous" forms, which I consider as theoretic and not really practical. He says: "Even very careful and anxious mothers usually notice nothing of a prodromal stage, and assert that their children were perfectly well during the days preceding the eruption. On the other hand, in some cases, also according to the statement of laymen, a real prodromal stage of some duration seems to have existed. My careful observations of numerous patients with especial reference to this point have shown that in most cases of varicella with ordinary, light, regular course,—normal cases,—a prodromal fever is not present or only one lasting but a few hours to half a day, and hence not important. I recognize that rare exceptions to this rule have been observed; as, indeed, in all children's diseases, a variable course is possible. According to my view, however, a prodromal fever of several days' duration in varicella is a variation from the normal course of the disease. When its presence as the rule is asserted by the defenders of the identity of smallpox and varicella, the suspicion that they are not considering true varicella is well founded, especially if the case is not in young children. But some who recognize the specific nature of varicella have also very exceptionally observed a fever of several days' duration, with severe nervous symptoms, even delirium and convulsions, and therefore the possibility that some cases run an anomalous course cannot be denied. But we must assert most positively that the normal and uncomplicated course of varicella is without a decided prodromal fever, an assertion justified by the fact that in these cases the eruption which appears later is often slight, and even resembles that in light and normal cases which run their course with normal temperature. Probably, then, this is not a true prodromal fever, but an accidental febrile complication, such as is so common in small children, but coincident with the beginning of varicella."

* In Gerhardt's "Handbuch," a. a. O. S. 328.

† "Lehrbuch der Kinderkrankheiten," S. 96.

‡ "Vorlesungen über Kinderkrankheiten," S. 688.

§ In v. Ziemssen's "Handbuch," a. a. O. S. 16, 17.

How much simpler it is to say that in light cases prodromal symptoms with more or less fever are lacking, but may occur in severe cases. As in all infectious diseases, besides elevation of the temperature, other symptoms of intoxication may be present in varicella, but this does not often happen. Probably it occurs even more rarely than the nephritis which may follow subsequently, and is due, as in scarlet fever and measles, to a poison generated by the pathogenic cause of the disease.

It is possible that some febrile disease may in these cases precede the outbreak of varicella. But I would not admit that the fact advanced by Thomas can be demonstrated. It is surely usual that, in variola weakened by a former inoculation which still lends some degree of protection, a considerable elevation of temperature lasting more than three days should follow the formation of a few pustules. Why should not something similar occur in varicella?

I might here give a very instructive observation of Kassowitz:*

"Emily Brodeman, a five-year-old, rather anemic girl, sickened during the night before the 13th of November, 1870, with high fever, general convulsions, and frequent vomiting. In the morning I found her in a deep sleep, broken at times by loud screams. About every quarter of an hour she was seized with cramps in the limbs, lasting two to three minutes and accompanied by slighter contractions of the face muscles. The eyes were fixed and the pupils slow to react. Respiration was irregular, of no fixed type; pulse regular, 126; and temperature, 40.0°. In the evening she was still unconscious, and recognized no one. Temperature, 40.2°. In the night there were some lucid intervals, in which the child complained of pain in the abdomen; there were no convulsions, but several attacks of vomiting.

"November 14th. Consciousness returned, the child answered questions slowly, the eyes staring, the pupils of unequal size. Temperature, 39.8°. During the day she again had several returns of cramps of short duration in the lower extremities and several fits of vomiting. She slept most of the time. When she was awakened, she answered unwillingly and fell asleep again. Beside the right nipple was a small vesicle, the size of a lentil, surrounded by a narrow red zone. There was no eruption on the rest of the body. Temperature, 39.8°.

"November 15th. In the night she vomited several times. The stupor continued. On the back are visible 6 to 8 spots, in part fully developed vesicles with clear contents, and in part dark red points, with central knob-like elevations. The contents of the vesicle on the breast are distinctly turbid. Temperature in the morning, 39.2°; in the evening, 39.4°.

"November 16th. Quiet night, consciousness in the morning. Many vesicles on the face and arms. The fluid in the vesicles on the back turbid. In the evening many new vesicles. Temperature morning, 37.6°; evening, 37.8°.

"November 17th. Morning temperature, 37.4°: evening, 37.8°.

* a. a. O. S. 167

"November 18th. Morning, 36.4°; evening, 36.8°. Most of the vesicles have dried. Many of the papules have not come to full development.

"November 19th. Most of the crusts have fallen off and all the vesicles have dried. Temperature, 36.6°."

Kassowitz adds: "The same girl, in August, 1872, passed through an attack of varicella under my care, in which she showed marked prodromal fever and delirium before the eruption."

This case teaches us that on suitable soil the pathogenic cause of varicella may cause symptoms of poisoning in no way less marked than those caused by the other infections. Such peculiarly susceptible people are rare, but there are such. It is analogous to those cases of scarlet fever and measles which are so quickly fatal.

A peculiar irritability of the brain may be seen. Disturbance of respiration with unconsciousness, convulsions, slow pulse, and trismus with subnormal temperature were seen by the Swedish physician Tham * in his own three and one-half-year-old daughter.

The further course corresponded to the usual course of the disease, and the sister, who was taken sick fourteen days later, had a mild attack of varicella.

Among the unusual prodromal phenomena is to be numbered the appearance of flatulent, uncontrollable, blood-stained evacuations from the bowels, which pass off with the eruption.

TEMPERATURE.

Some elevation of temperature seems to be always present, at least so far as our careful observations extend. I do not doubt, however, that in varicella, as in other acute exanthematous diseases, elevation of temperature may be absent.

Thomas,† who has made the most careful observations,‡ saw in 5 cases which were observed from the beginning, elevation to 38.2° (rectum). This is a slight but noticeable increase. These were all the very mildest cases.

In the other 46 cases the course of which Thomas followed carefully, he found generally a considerable elevation of temperature. He reports (measurements taken per rectum or reduced to the rectum

* "Jahrbuch für Kinderheilkunde," Neue Folge, Bd. xxv, S. 155, 156 (Referat).

† *Archiv für Dermatologie und Syphilis*, Bd. i, S. 335.

‡ I here follow Thomas. The more exact observations—measurements every two hours—which Rille published add nothing essentially new and are somewhat strictly kept. ("Beiträge zur Kenntniss der Varicellen." Aus der pädiatrischen Klinik der Prof. R. v. Jaksch in Graz. By J. H. Rille. *Wiener klinische Wochenschrift*, 1889, S. 733 ff.)

scale): To 38.5°, twice; to 39.0°, 11 times; to 39.5°, 15 times; to 40.0°, 10 times; to 40.5°, 6 times; to 41.0°, once. The maximum observed was 41.6°.

A decided relation between the skin affection and the temperature has not been shown. Rather, we must say that the local disturbance in varicella is, as a rule, independent of the general condition, so far as this finds expression in the temperature.

No definite fever type can be described, and only some general remarks are possible. The duration of the fever varies between one and seven days, and ends usually on the second and third days after the appearance of the eruption.

Generally the normal daily variations of temperature are retained, but disturbances may arise on the appearance of larger batches of the eruption.

Thomas * saw a case in which the eruption lasted about six days; the fever with intermissions not more exactly described lasted seventeen days and rose to 39.0°. "No marked local symptoms arose during this later fever." Nevertheless he remarks †: "Considerable anomalies of temperature, which sometimes occur during or even after the healing of the skin affection, are undoubtedly to be referred to newly arisen complications." I would unhesitatingly affirm that, regarding the after-fever, varicella is like the other acute exanthems, or, more correctly, the infectious diseases.

THE ERUPTION.

Sometimes, preceding the development of varicella, a wide-spread erythema involving nearly the whole surface of the body has been observed. Henoch saw this some hours before the eruption; Thomas,† about fifteen hours before. He describes the case more in detail; it was characterized by its high prodromal fever, 41.6°; but otherwise presented nothing remarkable.

The fundamental form of the varicella eruption is a circumscribed, bright flush, with slight swelling of the affected skin, and it therefore takes its place in the system-group of the roseolæ. Before proceeding to the further development, the papule should be mentioned. It is never the only or even the prevailing form; on the contrary, papules are found in far smaller numbers than macules, but it is incorrect to deny their presence, as is done by some.

Thus, Bohn ‡ says: "The vesicles never develop from a papular foundation, as in variola and varioloid." Thomas ‖ states: "I said that, as a

* a. a. O. S. 346 (Marie Kuanth, one and one-third years old).   † a. a. O. S. 351.
‡ a. a. O. S. 338 (Felix Schroter, two and one-half years).   § a. a. O. S. 329.
‖ In v. Ziemssen's "Handbuch," a. a. O. S. 14, and similarly in a. a. O. S. 332.

rule, the typical vesicle of varicella develops from a roseola, which is not at all or only slightly elevated, but never papular." In his histories of his patients, however, he especially mentions papules and the development of vesicles from them. Thus*: "On the face and other parts of the body vesicles have frequently developed from papules."

I would not injure any one, but I cannot avoid the impression that the desire to separate varicella morphologically also from variola has led these writers further than facts warrant.

Bohn also asserted that the vesicle of varicella is unilocular. So far as I know, he stands quite alone in this view. The simplest investigation, the pricking of the vesicle with a fine needle, shows ·that not all, but only a part, of the contents exude through such an opening. Before the vesicle is emptied, it is necessary to prick it several times and in different places. This was earlier asserted in general—as by Thomas: the multilocular structure of the vesicle, which is indicated by this test, has been shown anatomically by Unna.† He examined a "pointed pock," the form in its external appearance furthest removed from the umbilicated variola pustule: "These pointed pocks have a tent-like superstructure. From a broad base, the walls extend obliquely to the middle of the pock-roof, which consists of a small horny scale. From this, as in the pock of smallpox, compartment partitions extend to the floor. The waterpock is, like the pustule, divided into compartments, but the point of union of the septa lies not in the middle of the floor of the pock, but in the roof."

Unna gives a number of details which show that between variola and at least this simplest form of varicella vesicle there are great differences in the finer structure as in the pathologic changes in the tissue elements affected. I will not enter into this question here, as it would require too much space.

The contents of the vesicle are generally clear and light yellow in color. Later, they become slightly turbid and a few leucocytes are present. There may, however, be such a collection in the fluid that it cannot be distinguished from thin pus. When Thomas asserts that such thick pus as is found in the smallpox pustule is never seen in varicella, he is right, if we have in view the fully developed pock. But I believe that the contents of many poorly developed smallpox pustules seen in cases of mild infection are very similar to some of the pustules seen in severe cases of varicella.

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* *Archiv für Dermatologie und Syphilis,* Bd. i, S. 339.   Case of Martha Weber.

† "Die Histopathologie der Hautkrankheiten," Berlin, Hirschwald, 1894, S. 634.

It is the same with the formation of an umbilicus, the more indurated infiltration of the base and the area of inflammation extending somewhat beyond the local center. All this may be now and then observed in varicella in individual pustules—for these should no longer be called vesicles. I cannot admit either that the confluence of neighboring vesicles is "extremely exceptional," as Thomas says. It is true that often, indeed in the great majority of cases, the vesicles, singly disposed, are separated from each other by open interspaces, and remain so. But only in the cases with very scanty eruption does one seek in vain for confluent vesicles. I can assert this positively, for I have regularly noticed it. If I add to this that pitted scars may develop, in no way distinguishable from those which occur after smallpox, the corresponding morphologic properties of the two acute exanthems would be settled.

We have still to speak of other matters:

1. The extension of the eruption of varicella over the body with relation to place and time.

Generally the first changes in the skin appear on the scalp and, at about the same time, on the face. Exceptionally, they may appear elsewhere, oftenest on the trunk, most rarely on the limbs. No part of the body is spared, but usually the trunk is most affected, and the upper part more than the lower. But a very abundant eruption appears sufficiently often on the limbs, and, again, more on the upper portions than on the lower. The vesicles of varicella are seen on the palms of the hand and the soles of the feet; the head and face are generally less affected than the other parts of the body. In general, the eruption spreads from above downward.

Henoch has remarked that the skin, in places where it is exposed to greater mechanical irritation, presents more of the eruption. A similar fact may be noticed in variola vera.

It is also the rule that new vesicles may form in places already attacked, during the whole duration of the disease. They are, however, not so numerous, and the development of the macules into vesicles is not in this case so extensive that the distribution in that portion of the skin would be noticeably changed. It must also be stated that, according to the chronologic order, a weakening of the influence of the virus is evident; the centers of inflammation are not so numerous and not so large.

2. The history of the individual vesicle.

As to their duration: if they do not develop beyond the stage of

redness and slight swelling, they may heal perfectly in a very short time—in the course of a few hours. The macules which are found on the portions of the body earliest attacked are especially short lived.

The vesicle where it is especially profuse is perceptible within a few hours at longest of its origin. It is, as a rule, fully developed in one day at most, and tolerably often within a shorter time. It does not remain very long at its full height. It is difficult to assign exact periods for the whole process, but we may estimate the average time that the vesicle takes to develop from the beginning to its height at one day.

The retrogression shows itself by a decrease in the tension of the covering through its becoming relaxed. Whether the covering may burst in consequence of the pressure of the contents, I must, with Thomas, doubt. If the vesicle is not disturbed by scratching, the drying of the fluid progresses rapidly, at least in the smaller and medium-sized vesicles. After half a day to one day a dry, yellowish-brown crust, already becoming hard in the center, is seen in place of the vesicle, which is no longer surrounded by a reddened area. After a few days the crust falls off, and the slightly reddened skin remains, which soon assumes the color of the surrounding skin. As to the vesicles which contain a large number of leucocytes, or those which resemble the smallpox pustules, a longer period is to be reckoned for each phase, and, of course, a longer duration for their whole history.

The manner of retrogression is governed by the tissue disturbances. I have already reported on changes remaining in the affected skin.

The size of the vesicle in varicella varies within wide limits: From the size of a lentil, or even of the head of an ordinary pin (Thomas and Henoch speak of "miliary" vesicles), to that of a silver 20-penny piece,—that is, about 15 mm. in diameter,—we see them usually. But there are vesicles of the size of a dollar (thaler)—about 30 mm. in diameter.*

3. The number of varicella vesicles varies considerably. Thomas gives their number as 10 at the minimum and about 800 at the maximum.

4. The development of vesicles on the mucous membranes runs parallel in point of time to the development of these on the skin. The forms are also the same. But it should be stated that the far thinner covering of the vesicle is quickly destroyed under the influence

* See in Thomas, *Archiv für Dermatologie und Syphilis*, Bd. i, S. 342. Case of Theodore Schirmer, a boy of five years. The case was, on the whole, a mild one.

of its environment—warmth and moisture are always present. We see, therefore, superficial, circumscribed ulcers, deprived of epithelium and surrounded by a slightly reddened ring. The mucous membranes of the mouth and throat are regularly attacked, especially the hard palate, less often than the soft palate. Here I have seen them, and so has Thomas, at least very often; I do not remember exactly enough to say how often.

The mucous membranes of the mouth, lips, and cheeks are very regularly invaded, but the forms are here more indistinct, so that they are not with certainty recognizable. The tongue and lips may also be affected. Vesicles very rarely show themselves on the conjunctiva, even on the conjunctiva of the eyeball (Henoch). Thomas cites the following more frequent occurrences: The disease of the conjunctiva is continuous with one of the lids. The same may be found in the nasal cavities and in the mucosa of the nose itself. The mucous membrane of the vulva, and more rarely that of the prepuce, are attacked. On the mucous membrane of the larynx vesicles have exceptionally been found, but never, to my knowledge, on that of the trachea.

It is not very often that scratching causes the development of ulcers of long duration or gangrene in healthy children in parts of the skin affected by varicella. In the scrofulous it may more easily happen, but it is by no means an everyday occurrence. Of course, the reports coming from different circles of observation give different results. O. Vierordt * has more frequently seen these circumscribed gangrenes; Thomas,† never. He however cites older physicians, who have seen deep ulcers of considerable extent. According to my own observations, I believe that these occurrences are always the result of scratching.

SEQUELS AND COMPLICATIONS.

Henoch ‡ first taught that nephritis might follow varicella in the forms in which it follows other acute exanthems. Since then, such a number of observations have been published that the great frequency of its occurrence cannot be doubted. I myself have 2 cases on record. The kidney disease after varicella so perfectly resembles that after scarlet fever that the description there given will apply here. The transition from the light to the severe forms is found here also.

* In Pentzoldt-Stintzing's "Handbuch der speciellen Therapie innerer Krankheiten," Bd. i, S. 187.

† In v. Ziemssen's "Handbuch," a. a. O. S. 15.

‡ "Nephritis nach Varicellen." A pithy communication on four cases in the *Berliner klinischen Wochenschrift*, No. 2, of January 14, 1884.

Rille * describes a mild case, which, I believe incorrectly, he does not once point to as nephritis.

Högyes † reports a severe case, becoming fatal through pneumonia.

The nephritis after varicella has a similar prognosis to nephritis occurring after the other acute exanthems.

The other diseases reported as occurring after varicella—whether called sequelæ or complications—seem to me, at least provisionally, to have an extremely doubtful relation to varicella.

Rille, for instance, reports a pleuropneumonia of peculiar form, which developed in a boy of nine months, seventeen days after the last of the eruption of varicella, and in two days caused death. The exact measurements of temperature, as well as the careful observation of the patient, showed, except an unimportant elevation of temperature on the eleventh day before the attack of pneumonia, no disturbances in the condition of the boy. I consider it very venturesome to think here of a connection with the previous mild varicella, but not permissible to speak of a metastasis.

According to the report of Rille, Semtschenke saw in an epidemic at Kasan two cases, respectively of purulent pleuritis and purulent synovitis of the knee-joint, after varicella. The work has appeared in Russian, and hence is not accessible to the majority of western Europeans. But from the somewhat extended abstract in the "Jahrbuch für Kinderheilkunde"‡ nothing more exact can be gathered. On the other hand, I see from the communication of Laudon § that Semtschenke, by the inoculation of the varicella secretion into healthy children, is said to have produced smallpox in some cases. Whether in those cases his diagnosis was correct, may be doubted. Laudon himself reports an observation of his own of evident serous inflammation of the elbow-joint after varicella. The four-year-old boy was attacked at an early stage, while a part of the eruption was undergoing retrogression, amid marked febrile phenomena and perspiration, with pain in the right elbow-joint, to which considerable swelling was soon added. Only this one joint was affected. After some weeks, the recovery was perfect. The case is not to be doubted. The child, together with two sisters, was taken sick, all having been exposed during an epidemic of varicella. In all three, the usual form of the eruption occurred to the time of its height, and to its healing.

According to the work of Högyes, inflammation of several joints, beginning with sudden high fever (40.0°), occurred in a seven-year-old girl just as she was recovering from an attack of nephritis, which began eighteen days after the healing of the eruption of varicella. The first attack was of only short duration; after a complete intermission of six days, a second attack came on, from which also there was quick recovery. I do not know whether Bókai, who had reserved his deliberations on this case,

* a. a. O. S. 735.

† "Zwei Fälle von Nephritis varicellosa," "Jahrbuch für Kinderheilkunde," Neue Folge, Bd. xxiii, S. 337 ff.

‡ Neue Folge, Bd. xxv, S. 171.

§ "Varicellen mit Synovitis complicirt," *Deutsche medicinische Wochenschrift,* 1890, S. 567.

has come to a decided opinion.   To me, there seems to be no unqualified
necessity for assuming an immediate connection with varicella.   Nephritis
may have been the connecting-link.

DIAGNOSIS.

MOST of what is to be said here has already been mentioned.   I
will therefore satisfy myself with a brief summary.

If one can observe a case from the beginning, then the state of
the temperature is a weighty point for differentiating varicella and
variola, which is of the greatest importance in practice.   In respect
to this, two things should be stated:

1. The elevation of temperature preceding the eruption is far
greater and of longer duration in smallpox than in varicella.

2. With the appearance of the eruption in smallpox, the tempera-
ture falls to normal or below it.   This is a valid diagnostic for the
beginning of the disease; in the further course, the eruption is to be
especially observed.   However decidedly I have stated that in the
single pustule morphologic transitions from the varicella vesicle to
the pustules may present themselves which make it impossible to
assign with certainty the single pustule to one disease or the other,
yet I must state positively that the general picture of the diseases
is different.

We see in varicella, after a few days at the latest, the different
forms of development beside each other, chiefly red macules and
vesicles with a few papules.   The latter do not occur in varicella
without vesicles.   If they are present alone, then, in all probability,
smallpox is to be thought of.   But in smallpox the papules may be
wanting and only pus-filled vesicles may be found; it is always then
a very mild case with slight eruption.   Here a diagnosis may be
impossible.

The question of diagnosis is easier to decide if the patient has
passed the age of puberty.   In that case we must suppose that the
patient has true smallpox, and act accordingly.

Of course, we must take into consideration whether an epidemic
of varicella or of variola prevails, and whether we live in a region far
removed from intercourse with the outside world or not.   But this
point need not be discussed further.

As matters which should be considered in arriving at a differential
diagnosis, von Leube mentions pemphigus, which begins with fever and

may also attack the mucous membrane of the mouth. I must admit that, according to my own observations, a great similarity may exist at first. But the further course of the affection soon settles this difficulty. Pemphigus lasts much longer; for weeks upon weeks new vesicles form.

The so-called varicella syphilitica resembles varicella only superficially, and is easily recognized through the whole course of the disease.

PROGNOSIS.

IT may be described as very favorable. We should always add that, exceptionally, death may follow. In saying this, we should think especially of nephritis. Sepsis might possibly arise from infection of the ulcerating wounds made by scratching. Deaths from laryngitis are also mentioned. As varicella vesicles, as well as catarrhal inflammation, may be found in the throat, and even in the larynx, this should not be absolutely excluded.

Fürbringer * remarks that he has seen a child die of this condition in the midst of an undoubted varicella epidemic, without complications; so, probably, in consequence of infection.

This also is so rare an exception that we cannot in general speak of any serious danger to the varicella patient.

TREATMENT.

REALLY, it might generally be disregarded. A few days' rest in bed is usually sufficient. Only the appearance of certain symptoms calls for the help of the physician, which would then have to be given according to general principles. The severe itching is most frequently troublesome. Inunction with olive oil, or, if it becomes too severe, the application of oil-soaked fine linen cloths, is of great value. Prudence requires perhaps a frequent examination of the urine for albumin. The nephritis would have to be treated exactly like that occurring after scarlet fever.

* a. a. O. S. 22.

CHOLERA ASIATICA

AND

CHOLERA NOSTRAS.

BY

C. LIEBERMEISTER, M.D.

CHOLERA ASIATICA

AND

CHOLERA NOSTRAS.

CHOLERA ASIATICA.

HISTORY.

THE word cholera ($\chi o \lambda \epsilon \rho a$) is not infrequently met with in the most ancient writers on medicine (Hippocrates, Galen, Celsus, Cælius Aurelianus, and others), and was used by them to indicate a disease the principal symptoms of which were diarrhea and vomiting. Ordinarily the condition meant by them was what we call cholera nostras, or sporadic cholera, because Asiatic or Indian cholera, which occurs usually in great epidemics, was unknown to the Greeks and the Romans. A wide-spread epidemic in 1817 first drew the attention of European physicians to Asiatic cholera.

The disease appears to have originated in India. In the old writers of that country are to be found, under various names, descriptions of an epidemic and endemic disease that corresponds to our Asiatic cholera. Epidemics are also described by Europeans—especially Portuguese, Dutch, French, and English traders who visited the East Indies in the sixteenth century—some of which seem to have been undoubtedly this disease. There is likewise no doubt that before 1817 cholera sometimes outstepped its Indian boundaries, and appeared in Ceylon and Java. The precise home of the disease, where all epidemics originate, is Hindoostan, and in that country especially the lowlands of Bengal near the mouths of the rivers Ganges and Brahmaputra.

In 1817 the cholera in India prevailed to a greater extent than ever before. In the years 1819 to 1823 it passed the confines of the peninsula, raged on the islands of the Indian Archipelago, and spread

in one direction to Persia and Arabia, in the other to China and Japan. In this epidemic the disease crossed for the first time the boundaries of Europe, and appeared in Astrakhan on the Caspian Sea (September, 1823); though it disappeared thence in a short time with the approach of a cold winter. After it had again become epidemic in India, in 1826, it overstepped the European boundary for the second time, reaching Orenburg (August, 1829) and Astrakhan (July, 1830). Thence it spread gradually westward to Moscow (September, 1830), Warsaw (April, 1831), Berlin (September, 1831), Hamburg (October, 1831), and Paris (March, 1832). ·

At the same time this epidemic appeared in the British Isles and was carried by Irish emigrants to America, where it broke out for the first time in Canada (June, 1832). In this and the following years up to the winter of 1837–38 it spread over the greater part of those countries which were in commercial communication with each other. After this came an interval of almost ten years during which all countries outside of Asia remained free from the pest.

A third epidemic, originating again in India, reached Europe in 1847, and during more than ten years spread over the eastern and western hemispheres. Its most wide-spread prevalence was during the years 1849, 1850, and from 1853 to 1855.

The fourth pandemic struck Europe in 1865. The disease was carried to Mecca by Indian pilgrims, and the dispersion of these spread it in all directions. It reached Europe by way of Egypt. Its greatest prevalence was in the years 1865 and 1866, and again in 1872 and 1873. From 1877 to 1879 it still prevailed in Japan; but, with the exception of India itself, it had died out of all other countries in 1875.

A fifth epidemic began in the early eighties, and the disease arrived in Europe in 1884. As early as 1881 and 1882 it had already shown itself in Mecca, having again been brought thither by Indian pilgrims. In the summer of 1883 it raged in Egypt, counting more than 28,000 victims. In the summer of 1884 it struck Toulon and spread over southern France, Italy, and Spain. It was still very prevalent in Italy in 1886 and 1887, and in 1886 it appeared at Trieste and in Hungary. It was carried to South America by an Italian ship, played havoc in the Argentine Republic, and succeeded in crossing the Andes to Chili. Only a few more or less isolated small epidemics appeared in Germany at this time (1886) (Gaffky, 1887). (See the Bibliographic Index at the end of this section.

In the five years from June, 1887, to June, 1892, cholera continued

prevalent in Asia, but in other countries larger epidemics were found only in Argentina and Chili (1888) and in Spain (1890).

In the year 1892 a notable outbreak occurred in Afghanistan and in Persia. In these places the disease had remained endemic and had assumed an epidemic form each summer. At Baku on the Caspian Sea, the Russian port for Persian trade, a severe epidemic broke out in June, and the flight of the inhabitants disseminated it in various directions. By the second half of July it had reached Moscow and St. Petersburg, and was spreading gradually westward.

At even an earlier date, in the spring of 1892, the disease appeared in the neighborhood of Paris. Whether it was carried thither or, as has been suggested, the germs derived from an earlier epidemic had remained alive has not been determined. In July it entered Paris, and at the same time reached Havre, where an epidemic arose.

For the first half of the year 1892 it held aloof from Germany, but then suddenly and unexpectedly it appeared at Hamburg in so frightful a form that from August 16th to November 12th, 16,956 sickened with the disease and 8605 died. Later, after it had seemingly departed, two small satellite-epidemics broke out, one in December, 1892, the other in September, 1893.

In what manner the disease reached Hamburg has not been determined; though as a matter of fact a considerable shipping trade existed both with Russian ports and with Havre, not to mention large crowds of emigrants of the lowest classes from Russia to America who passed through Hamburg at this time. The number of these emigrants during the month of August alone was about 5500.

From Hamburg the disease spread widely, but the immediate suburbs of Altona and Wandsbeck suffered most. In Altona 572 persons sickened, of whom 328 died; in Wandsbeck there were 64 cases with 43 deaths. During the year 1892 cholera broke out in 267 places in Germany, most of these outbreaks being directly or indirectly connected with the Hamburg epidemic. Yet in most of these places only isolated cases appeared, excepting at the Nietleben Insane Asylum at Halle, where a comparatively large epidemic broke out in January, 1893. The different places attacked, together with the number of cases and deaths, are recorded in the weekly returns of the Imperial Board of Health, collected together in the "Denkschrift über die Cholera-epidemie," which was laid before the Reichstag. (See Bibliographic Index.) If we except Hamburg, Altona,

and Wandsbeck, the total number of cases reported in the year 1892 from 264 different places in Germany was 1048, of which 607 died.

In 1892 and in the following year cholera appeared in many other European countries, but in most places only in the form of localized outbreaks. In Russia alone were great epidemics seen, as in Podolia and especially in Wolhynia. Moreover, in 1894 there was a considerable outbreak in Galicia, and even in 1895 cases were still met with. In Constantinople also cholera seemed not yet to be extinct, but the other European countries had no considerable epidemic in 1895.

In Germany in 1893 the total number of cases was 915, the number of deaths 396. In 1894 cases were still occurring, especially in the east along the Russian border, so that 157 places reported the disease, with 1004 attacked and 490 deaths. In 1895 no cases were reported.

In Asia in 1895 cholera extended over (besides India) Japan, China, Persia, Arabia, and Asia Minor. In Africa small epidemics appeared in Egypt, in Morocco, and in French West Africa. In America the disease limited itself to the La Plata States and Brazil.

A careful grouping of reports of the two first epidemics, together with charts, may be found in Riecke's article. (See the Bibliographic Index.) For the history of cholera to the year 1859 see Drasche (1860); to 1880, see Hirsch (1881). The distribution of cholera in Germany in 1892 is described in the "Denkschrift" mentioned above. A good grouping of the histories of epidemics is given by Petri (1893). Exact reports as to the appearance and progression of the disease in different countries and the proportion attacked will be found in the publications of the Imperial Board of Health ("Veroffentlichungen des Kaiserlichen Gesundheit-samts").

ETIOLOGY.

THE MICROBES OF CHOLERA.

The cause of cholera is a specific pathogenic micro-organism that invades the intestine and there develops.

A considerable time before the actual discovery numerous observers had come to the conclusion that the fomites of the virus of the disease were to be found in the stools or the vomit of cholera patients. Attempts to isolate the poison by chemical means were without result. Likewise, the animal and vegetable micro-organisms ("Cholerathierchen und Cholerapflanzen") which were discovered from time to time were proved to be accidental admixtures. Of greater importance were the observations of Pacini (1854), who found with high microscopic powers in the mucous flocculi of cholera stools large numbers of very small, markedly motile vibrios. [In 1838 Ehrenberg described four genera of filamentous bacteria—which he wrongly regarded as unicellular animal organisms, *Infusoria*—under the heading Bacterium, Vibrio, Spirillum, and Spirochæte. In more modern times the term Vibrio was used to designate a genus of Schizomycetes, or fission-fungi, having cylindric, curved, or spirally wound cells with a cilium at each end. The micro-organism of cholera, however, is more correctly referred to the genus Spirillum, and Sternberg calls it *Spirillum choleræ asiaticæ*. R. Koch (1884) called it *Kommabacillus der Choleræ asiaticæ*, and after him it is generally known as the "comma bacillus of Koch."]

Similar observations were made later by other investigators. Leyden (1866, see Wiewiorowski) found on microscopic examination of cholera stools "vast numbers of bacteria and vibrios which it was impossible to conceive were unimportant or accidental, since they formed the principal part of the 1 or 2% solid constituents of the evacuations. Under the microscope these bacteria showed lively movements, often so marked that they resembled a swarm of gnats. The dejecta of other diseases presented no such picture; these peculiar forms being seen in cholera alone."

J. Klob (1867) found in the stools of cholera patients, and in the intestinal contents of those dead of the disease, great numbers of small round and rod-like forms, some motile, some not, which

were aggregated into masses (zooglea) by means of a gelatinous sub-
stance.   The supposition that these might prove the cause of cholera
had scarcely been brought forward before similar micro-organisms,
or at least ones that could not at the time be differentiated from
them, were found in other severe diarrheas, and even in isolated
cases of arsenic-poisoning (Virchow, C. E. E. Hoffmann).   Other
observers found, in the blood, forms which they believed were the
microbes of cholera.

The bacilli or spirilla of cholera have a length of 1 to 1½ micro-
millimeters.   An idea of their size may be gained by realizing that it
would take from 700 to 900 of them, end to end, to reach the distance
of a millimeter.   They are considerably smaller than tubercle bacilli,
but much plumper and thicker.   They are usually not straight, but
somewhat curved, resembling a comma, and sometimes they form a
half circle.   In cultures they sometimes hang together in twos, making
S forms; or they may even appear in long threads twisted like a cork-
screw and simulating spirilla.   They are motile, and in a hanging
drop are seen swarming actively across the field.   A single flagellum,
discovered by Löffler, is responsible for this motility.   The flagellum
is attached to the end of the bacillus and is of considerable length.
These organisms are found in the stools, and rarely in the vomit, of
cholera patients.   Postmortem they are found in large numbers in
the intestinal contents, often almost in pure culture; also in the intes-
tinal wall, but usually not in the stomach.   As a rule, too, they are
sought for in vain in the blood and other organs of the recently
deceased.

The cholera bacilli develop and multiply in various media (bouil-
lon, milk, blood-serum, peptone solution, gelatin, agar).   They thrive
best in weak alkaline solutions and at a temperature from 30° to 40°
C.; less well at a lower temperature, though they will stand freezing
for a short time without dying.   A higher temperature, about 60°
and over, kills them rapidly.   On the cut surface of cooked potato
at a temperature of 30° to 36° C. they develop in the form of a thick,

yellowish-brown growth. In other nutritive media they may remain alive for many days.

The resistance of the organisms as they are found in the stools, the intestine, or even in cultures on the ordinary media, is slight. They will not develop in acid solutions, and it requires but a small amount of acid to kill them. The ordinary germicides act quickly on them, and desiccation very quickly causes their death. In the struggle with other saprophytic organisms they prove the weaker. In ordinary water they are easily overgrown by other bacteria, but they preserve life longer if the water has been previously sterilized. In manure or sewage they die quickly. The intestinal contents or stools of cholera patients on moist earth or when spread out on linen and kept moist show at first an extraordinary increase in the number of bacilli, but after a few days they usually begin to die and other bacteria, which up to this time were overgrown by the comma bacilli, gradually get the upper hand.

When grown on suitable media the dried organisms contain 65% albumin and 31% ash (Cramer).

The most important biologic characteristics of the bacilli were determined in India by the Commission over which R. Koch presided. Especial attention was paid to the question as to whether there was a form of the organism that would resist drying. In spite of the most careful search, no such form was found.

While the characteristic bacilli never failed to appear in 42 cases of cholera examined after death in India, in 30 autopsies on victims of other diseases they were never present, though the examination was carried out in exactly the same manner. The examination of stools of non-cholera patients, and of animals also, proved negative.

The method of obtaining pure cultures from the intestinal contents in the dejecta has been described by Gaffky (1887) in the report of the work of the Commission as follows: "A small mucous flake is introduced into, and first of all thoroughly mixed with, about 10 c.c. of a 10% nutrient gelatin (bouillon-peptone-gelatin mixture, containing 10% gelatin, and of weak alkaline reaction) which has been previously liquefied by slight warming. From this first tube, a second is inoculated, and from the second a third, in order to obtain different degrees of dilution, so that at least one tube will have the organisms so separated from one another as to make isolation possible. The contents of the three tubes are now poured on to a glass plate placed horizontally and cooled by underlying ice. As soon as the gelatin becomes hard, the plate is put under a moistened glass bell between two plates lined by moist blotting-paper, in order to prevent too rapid desiccation. In twenty-four hours the gelatin shows small points, each one of which corresponds to a pure culture of micro-organisms.

"In very acute cases it is not uncommon to find cholera bacilli almost alone on the plates; while in cases of a more chronic character, or in which the acme of the disease is already past, besides the cholera bacilli, more or less numerous colonies of the ordinary intestinal bacteria are found. Yet

the colonies of cholera bacilli are so characteristic under low powers of the microscope that they can always be easily recognized, and can be transferred without further trouble in pure culture to other media in order to prove their identity. With a low-power lens and after twenty-four hours' growth in gelatin a colony of cholera bacilli appears as a small pale drop, which is not exactly round, like most bacterial colonies that grow in gelatin, but is irregularly limited, more or less star-shaped, and of rough or uneven contour. Quite early, too, it takes on a granular appearance different from the homogeneous character of other colonies. As it grows larger this granular character becomes more evident. Finally it seems to consist of innumerable strongly refractive granules, which the head of the Commission likened to a heap of finely ground glass. On further growth the gelatin liquefies in the immediate neighborhood of the bacterial colony, and the latter sinks simultaneously somewhat into it, so that a small funnel-shaped depression is made, in the middle of which the colony is seen by the naked eye as a white point. This liquefaction of the gelatin proceeds so slowly that, provided the colony is sufficiently isolated, it serves as a characteristic by which, even after many days' growth, the colony may be differentiated from the many others that liquefy gelatin. The macroscopic appearance of a gelatin plate containing numerous young colonies of cholera bacilli lying close together is likewise characteristic, its surface resembling that of a ground-glass plate. Not infrequently young colonies show, besides, as a result of the slight difference of level due to the sinking down of the surface of the gelatin stratum, a light reddish appearance in certain lights. The sinking down of the colony and the characteristic funnel formation can be followed with greater facility in a gelatin stab culture. Here the cholera bacilli are seen developing along the line of inoculation as a grayish-white film, and at the upper end a small funnel-shaped depression forms. On account of liquefaction occurring more rapidly at the top than along the rest of the stab, the line of growth soon appears to be capped by a small air-bubble, at the bottom of which is seen the colony. Moreover, the grayish-white line along the needle track no longer appears continuous, as in the beginning, but consists of many isolated flakes separated from one another by clear gelatin. Very gradually and slowly liquefaction continues, at first more marked at its upper part, until in from one to two weeks, depending on the temperature, the entire gelatin is liquefied. When this occurs, the great majority of organisms sink to the bottom as a grayish-yellow stringy mass; the uppermost part of the liquid remains slightly cloudy, due probably to bacilli still in motion, and the liquid gelatin between these two layers becomes gradually clearer.

"In agar a grayish growth, changing later to light yellow, also takes place, but without any liquefaction of the medium.

"The bacilli thrive well in fluid and on solidified blood-serum, the latter being gradually liquefied, at high temperatures (30° to 40° C.) more rapidly, at low (about 18° C.) more slowly. In milk, development is also rapid, and, what is remarkable, there is no coagulation or other macroscopic change.

"Neutral or weakly alkaline bouillon makes an excellent medium. In a hanging drop in this medium the bacilli exhibit wonderful motility. At the margin of the drop, where they are most active, they resemble a swarm of dancing gnats. Among the bacilli the corkscrew forms display the same liveliness of movement."

That these bacilli discovered by R. Koch were the only and sufficient cause of cholera was at once recognized by those investigators who had previously concluded that the exciting cause of cholera must be a microparasite (see author's paper, "Ueber die Ursachen der Volkskrankheiten," Basel, 1865). Yet the fact that Koch's bacilli were found, as a rule, only in the intestinal canal, and not in the blood and other organs,—a circumstance which in the case of many physicians drove them from their preconceived opinion,—must by impartial observers who rightly estimate the symptoms of the disease be accepted as a further ground for regarding these bacilli as the essential cause of the malady.

Naturally, doubt and controversy did not fail to appear. Apart from cholera patients, bacilli were found that corresponded closely with Koch's, as in the evacuations of patients with cholera nostras (Finkler and Pryor), in the intestinal contents of others with other diseases and even of healthy people, in many decomposing fluids, in standing and running water, in the contents of the mouths of the healthy and the sick. As a matter of fact, the further bacteriologic investigation proceeded, the more common became organisms that were with difficulty differentiated from the true cholera bacilli. Yet in every case more exact investigation proved that differences did exist, if not in form, then in development, or in growth on different media, or in the reaction of pure cultures toward chemical reagents, or in infectiousness or other characteristics; and so eventually Koch's bacillus came to be absolutely recognized as a specific organism, to be found only in cases of Asiatic cholera.

Further study brought to light the fact that even in true cholera the bacilli may show differences in their behavior. And this led Dr. Cunningham, in Calcutta (1892), to believe that in cholera it was possible to differentiate many various types of bacilli. Many cultural deviations were also found in different localities and in different media. But all these variations are so slight that we are not obliged to look upon them as different species of the cholera bacillus; they should rather be looked on as different varieties or species similar to those seen in other organisms under special conditions. "The cholera vibrios represent a definite species, the variability of which is not greater than that seen in other bacteria" (R. Pfeiffer 1895; see also P. Friedrich, 1893).

The most remarkable opposition was raised by von Pettenkofer and his school. For ten years von Pettenkofer taught that the danger was *nil* if a simple micro-organism was to be considered the

sole cause of the disease. Under such circumstances the obstinacy of the controversy can be understood. The attempt to make, not Koch's bacillus, but a micro-organism of an entirely different kind, the so-called Neapolitan bacterium, responsible for the disease (Emmerich 1884, Buchner 1885) failed completely. [The colon bacillus —*Bacterium coli commune*—of Escherich was obtained by Emmerich in 1885 from the blood, internal organs, and evacuations of cholera patients at Naples. Hence this micro-organism has been called Emmerich's bacillus, or *Bacillus neapolitanus*. This bacillus is now called *B. coli communis*.] The opposition, therefore, saw itself obliged to give up one position after another, and finally to allow that Koch's bacilli were important in the etiology of cholera and even indispensable for the production of the disease. Yet it did not acknowledge them to be the all-sufficient cause; on the contrary, it affirmed that something additional was required. According to von Pettenkofer's newer formula, to the bacilli X must be added a Y, namely, a predisposition brought about by season and place or locality, and likewise a Z, representing the individual susceptibility. This view, of the truth of which von Pettenkofer was so convinced that he endangered his life by swallowing a pure culture of comma bacilli, contains undoubtedly a kernel of truth, and we will revert to this subject. On the whole, however, the question of the specificity of the bacilli remains the same. We must, therefore, pronounce Koch's bacilli to be the specific cause of cholera.

Still, it is an error to believe that with this conclusion the etiology of cholera is settled. A series of questions still remains which in the present state of our knowledge can be answered only in part.

Cholera exhibits in its spread striking differences, inasmuch as we sometimes see only isolated cases, at another time a larger or smaller epidemic. Moreover, for this difference in behavior there is often no evident cause, so that it is not uncommon to speak of "the caprice of the disease." Added to this is the slight power of resistance of the comma bacillus to acids, to desiccation; its weakness in the struggle with simultaneously existing saprophytes—a circumstance which prevents its relation to the origin of the disease being apparent at first sight.

CONTAGIOUSNESS.

Since cholera was first recognized, discussion concerning its contagiousness has never ceased. Even to-day different opinions prevail as to whether the conclusion of Koch or that of von Pettenkofer

merits the greater consideration. This strife between those who believe it contagious, and those who insist on a necessary predisposition due to locality, is practically a continuation of the old discussion as to its contagiousness or non-contagiousness. Both sides, those who contend for contagion and those who oppose it, ground their arguments on facts.

Whoever has even only partly studied the way in which cholera spreads must realize that the disease is not contagious, in the sense of the ordinary contagious diseases, as smallpox, measles, scarlet fever, and typhus. These diseases are transferred from person to person, and in order to acquire them it is necessary to come directly or indirectly in contact with a patient. As a consequence, epidemics of these diseases are independent of season, weather, and temperature. Cholera, on the contrary, is so strikingly dependent on these external conditions that a connection between them and the spread of the disease cannot be doubted.

Contact with cholera patients is but slightly dangerous. Physicians and nurses are scarcely more frequently attacked than other people. On the other hand, numbers acquire the disease who never came in contact with, or even saw, a cholera patient. Inoculation with the blood, secretions, and excretions of cholera cases has proved negative. Even swallowing of the vomit, as was done by certain physicians during the first European epidemic, gave no results. Such experiments as these during the first epidemic caused most medical men who had had much to do with cholera to declare in favor of its non-contagiousness.

Recent experiments have enriched this question with new facts, but they have not brought it any nearer to a settlement. It has been proved that the swallowing of pure cultures of cholera bacilli is in many cases harmless. Yet this is not wonderful when we reflect that ordinary cholera micro-organisms are quickly killed by acids, and that, consequently, an individual with normal gastric juice might with impunity try such an experiment. In animals also we have found that the introduction of cholera dejecta or of pure cultures of the bacilli by way of the stomach produces, as a rule, no morbid effect; yet if, avoiding the stomach, the organisms are injected directly into the duodenum, a serious disease is brought about (Nicati and Rietsch, R. Koch, van Ermengem, and others). Somewhat similarly in human beings, if the gastric juice is neutralized, the same result follows. This was shown in the cases of von Pettenkofer and Emmerich (1892), who swallowed large quantities of a pure

culture in bicarbonate of sodium, with the consequence that symptoms corresponding to a light cholera attack were produced, and comma bacilli in large numbers appeared in the stools. Similar results were found by other investigators (Metschnikoff, Hasterlik). This makes it very likely that the introduction of the bacilli into the stomach of a person whose gastric juice is continuously, or at least temporarily, deficient in hydrochloric acid will produce the disease. As a matter of fact, several cases are recorded of physicians acquiring the disease by careless handling of the organisms in bacteriologic laboratories. From this it is to be inferred perhaps that food or drink contaminated with dejecta of cholera patients might, under particular circumstances, be dangerous, though this mode of transference must be rare, because such uncleanliness is uncommon even among the lowest classes.

It is also remarkable that in the numerous cases in which bacilli were introduced experimentally, or in which an accidental infection took place in a laboratory, the disease was so mild as to make it often doubtful whether it was true cholera or not. So far there has been only one death reported from such an infection (Reincke). The reason for this is considered to be the lessened virulence of the bacilli.

Therefore we can conclude that, even though cholera may be transferred directly from person to person, this is by no means the ordinary manner by which an epidemic spreads. And, furthermore, if an accidental case should occur from carelessness in handling the bacilli or the evacuations, this is not sufficient to bring about an epidemic.

AUTOCHTHONOUS ORIGIN.

It is beyond dispute that cholera can never arise spontaneously. It can occur in a locality outside of India only if it has been introduced there.

True, it is not possible in many cases to show exactly how and when this introduction took place, and in the past under these circumstances it was popularly considered that the disease must have originated spontaneously. Of late we have become more cautious in drawing such an inference. It is practically impossible to review all the ways of communication, therefore any conclusion in relation to this must be uncertain. Of especial importance in this regard was the discovery that the disease might be disseminated not alone by patients seriously attacked, but by very mild cases, and even by persons apparently well. Moreover, under particular circumstances

linen and clothes in general, food, and other fomites may convey the germs of the malady. To shut out the possibility of its introduction under such conditions would require that all traffic of persons and goods should completely cease.

On the other hand, there are numerous cases in which the manner of introduction is so well known that the person can be named who carried the disease to the previously non-infected region. When I was assistant physician to the hospital at Greifswald in 1859, cholera was introduced by a child who was brought into the surgical clinic to be operated on for harelip. The child came from Stralsund, where cholera was then raging. It died a few days after admission, with vomiting and diarrhea. A nurse associated with this surgical clinic was the first case infected, but from this case it spread through all the wards of the hospital, and even through the city. And this example is very typical, since it is not uncommon for epidemics to arise through very young children suffering from an unheeded attack of vomiting and diarrhea.

That the disease is spread by the means of traffic is proved by the history of the epidemics. As far as historic knowledge extends, there was no cholera epidemic outside of Asia before 1817. Before this time, therefore, the telluric and cosmic conditions necessary to its origin must have been wanting. But since it began, it has been disseminated over the earth in every direction of traffic, without partiality for race or country. Yet it has never spread more rapidly than the facilities of communication would warrant. At the time of the first epidemic, when means of travel were slow, the disease spread slowly; on an average, not further than the distance that could be accomplished in a four hours' journey daily. To go from Astrakhan to Paris in its necessarily roundabout way, and with frequent interruptions, required from August, 1830, till March, 1832. That this snail-like advance was due to the slowness of intercommunication becomes very evident from the experience of the present day. In our time cholera travels with our more rapid means of transit. From Alexandria to Ancona, and from Odessa to Altenburg, in 1865 only as much time was consumed as was required for a steamboat to make the trip between those points. In 1867 it traveled from Rome to Zürich in four days, and now it can be carried from St. Petersburg to Paris with the swiftness of the express train.

A further proof is drawn from the fact that in their spread epidemics always follow the line of travel. If this changes, the path of the spread of cholera changes with it. The first pandemics came

to Europe by way of the caravan routes from India over Afghanistan
and Persia; now the cholera route is usually by way of the Red Sea
and the Suez canal; only occasionally (1892) does it follow its old
highway. The direction of the wind and the course of the currents
of great rivers has nothing to do with it; so far as traffic takes place
in both directions, cholera spreads as easily against the stream as
with it. In America and other countries separated from epidemic
foci by the ocean it never happens that cholera appears first in the
interior, but always in the ports where ships arrive from infected
regions. These facts have led most physicians to declare in favor of
the contagiousness of cholera.

THEORY AS TO HOW CHOLERA SPREADS.

We must conclude, therefore, that cholera does not, as a rule,
spread from person to person, and also that it does not originate
spontaneously or through an autochthonous miasm.

The task which lies before our theory is to make these facts corre-
spond, and to find a solution for the apparent contradiction contained
in them—namely, that, although cholera is undoubtedly an infectious
disease, it is neither contagious, in the ordinary sense of the word,
nor miasmatic. Von Pettenkofer, the master of the school that in-
sists on locality as being the most important predisposing factor,
and the most violent antagonist of the contagionist doctrine, has
given no theory that is more than in some degree satisfactory. His
numerous papers, rich in circumstantial detail on the epidemiology of
the disease, comprehend a great number of facts, yet they are to be
admired more for their witty and ingenious logic than for their im-
partial consideration of the facts. Many of von Pettenkofer's con-
clusions have been negatived by the lapse of time, and the positive
propositions in his theory can scarcely be said to prove much more
than that the predisposition imposed by season and locality plays the
principal rôle, or that a special condition of the ground, or something
emanating from the ground, is necessary for the originating of the
disease. What this condition of the ground may consist in, and how
it may effect the origin of the disease, are questions that remain
unanswered. As a matter of fact, the endeavor to formulate this
theory with anything like exactness is hopeless.

Nägeli (1877) made the attempt to clothe this theory in a more
scientific dress, by shrouding it in scientific mystery. As an authority
on lower bacterial forms, which he presumed to be the cause of all

infectious diseases, he undertook to bring into accord these epidemiologic contradictions. But his knowledge of epidemiology was defective, and he had already come to the conclusion that von Pettenkofer's teaching in regard to the etiology of infectious diseases was incontrovertible. He brought forward the "diblastic theory," or theory of double cause, by assuming that cholera originated from the combined effect of a contagium derived from a diseased case, and a miasm emanating from the ground. Both the contagium and miasm he considered to be micro-organisms. This hypothesis, which seemed to explain in a very simple manner the occasional contagious and miasmatic character of the disease, was later defended by Buchner, who suggested that the ground micro-organism might be a protozoon. In like manner other investigators have referred the origin of cholera to a reinforcement of Koch's bacillus by other micro-organisms. With respect to these and such like hypotheses, it must be conceded that there are many epiphenomena met with in cholera patients which are the result of mixed infection, but that cholera arises only by this means is an unwarrantable presumption, totally unsupported by facts.

According to my opinion, the difficulty of bringing the facts into accord lies in the old assumption that an infectious disease must be either contagious or miasmatic. If this view is rejected, the solution of the apparent contradictions is easy.

As far back as the year 1865, under the supposition that all infectious diseases were due to the invasion and development of micro-organisms, I endeavored to make the seemingly contradictory facts in relation to the epidemiology of cholera agree, by assuming that its microbes required for their development two different stages. "We see a complete analogy to this in many organisms that act as parasites in the human being. The round-worm, for instance, cannot be transferred from person to person. The actual introduction of its mature eggs into the intestinal canal is insufficient. It develops in its human host only when introduced after a certain stage in its development has been passed. This condition, known with certainty for the round-worm, is repeated in analogous or slightly modified ways, in a number of the lower animals and plants; that is to say, their reproduction requires that they should pass through different stages in different habitats. And if we assume this theory in the case of the cholera micro-organism, and maintain that it has two necessary stages in its life history, one within and one without the human body, the difficulty which the interpretation of the facts offers is entirely solved.

The fresh evacuations of cholera patients contain these organisms in that stage of their development in which they can be introduced into a man without reproducing themselves and causing any sickness deserving of the name of cholera; before they further become capable of causing it they must pass through the second stage of their existence outside the body. This latter takes place if the evacuations are allowed to remain standing for some time, especially if they are in contact with a great quantity of easily decomposed organic matter, as happens in latrines, dung-heaps, sewers, or in soil saturated with water and rich in organic debris. In this developmental stage there seems to be a considerable intensification of the virus, and only after this increase in virulence is the latter in a condition to cause disease again if introduced into the human body. Thus it becomes clear how a pronounced case as well as a mild one may be the cause of an epidemic, if the dejecta remain exposed under conditions favorable to the development of the virus." (" Ueber die Ursachen der Volks-krankheiten," Basel, 1865, page 28 *et seq.*)

The first part of this hypothesis, namely, that cholera is caused by a specific micro-organism, was confirmed by the discovery of R. Koch. The second part, that this micro-organism must pass through another stage of evolution outside of the body before it can cause the disease, has been denied by R. Koch. Yet I am still of the opinion that cholera does not usually arise from bacilli as they are found in fresh feces, with their slight powers of resistance to acids, to desiccation, and to many other influences. On the contrary, I more than ever insist that the bacilli must, as a rule, take on a more resistant form in order to be capable of infecting man.

When F. Hueppe, in 1885, announced that he had found a stable form of the cholera microbe in the shape of an arthrospore, it looked as if the question was settled, and according to my previously expressed opinion. But this announcement proved to be premature. After Hueppe had acknowledged his error, he suggested (1890, 1891) that the cholera micro-organisms are less resistant to external influences after their anaerobic life in the intestine as a result of a deficient formation of their membrane. Therefore, in the condition in which they leave the intestine they are but little prepared for direct transfer, and for this reason cases of direct contagion are decidedly the exception. But bacilli grown aerobically outside the body become more resistant to external influences, and are therefore more competent to cause infection. The transfer is then an indirect one, and consequently, to a certain extent, the disease may be described as mias-

matic. This hypothesis also will conform to all the epidemiologic facts.

I doubt not that future investigation of the old feud between those who believed in contagion and those who opposed it, and likewise of the later discussion between the former and those who insisted on the predisposition due to locality, will settle it according to the theory that I ventured to express in 1865—namely, that cholera is not, as a rule, directly transferred from one person to another, but that the micro-organism from a case is deposited where it can attain the special conditions necessary for its development, and thus alone become capable of inducing the disease in others. For this development outside the body and for this increase in power to infect certain conditions in the surrounding medium are required, such as its temperature, its capacity for moisture and air, and the presence of certain organic and inorganic substances. These conditions are of such importance that on them depends whether, supposing the disease has already been introduced, an epidemic will arise or not, or whether this will be of greater or less extent. These conclusions support the theory of predisposition of locality, in so far as it is based on facts.

Since cholera is not transferred by contact,—at least, as a rule, not directly from man to man,—it cannot be called contagious; on the contrary, since the organism arises from without, it must be designated miasmatic. Still, in a broader sense it is contagious, because the micro-organism always comes indirectly from a previous case. Therefore for this disease, as well as those others that behave in a similar way,—enteric fever, dysentery, yellow fever, and plague, —I have (1865) employed the word miasmatic-contagious.

Even before 1865 this term had been used, but ordinarily only as a compromise between those who believed in contagion and their opponents. Such compromises, though they are to be recommended in practical matters, cannot be permitted in scientific considerations. My employment of the expression, on the contrary, is for the purpose of greater exactness, so that the name may correspond with the facts.

Therefore, for the present the conditions necessary to the origin of a cholera epidemic may be stated somewhat as follows: *a cholera epidemic may arise in any place where cholera bacilli from a patient sick with the disease find a culture-ground on which they can properly develop their infectious form and from which they can invade the intestinal canal of others.*

This theory supports those who believe in contagion as well as those who insist on the predisposition of locality, in as far as their

assertions are based on facts. It corresponds to R. Koch's views that the comma bacillus is the specific cause of cholera. It agrees with those of von Pettenkofer, inasmuch as the bacilli which he recently acknowledged as the peculiar cause of the disease, and designated X, are not alone sufficient to bring about an epidemic, but need besides a Y, or special culture-ground where they can develop to the proper form, and a Z, or susceptible person. A cholera epidemic is, then, in a certain measure, the product of three factors—X, Y, Z. If one of these is wanting,—in other words, if it equals 0, —the whole product becomes 0.

The question as to what constitutes Y, or the factor that brings about the development of the bacilli into the form in which they are infectious, cannot be fully answered. We can assert that to become infectious the bacilli must obtain greater powers of resistance and a higher degree of virulence. That the power of resistance is dependent on the culture-medium and other circumstances is conceded by all. In many micro-organisms the degree of virulence is subject to wide fluctuations. I need mention only the Streptococcus pyōgenes and the diphtheria bacilli. And for the cholera microbes we already know different circumstances by which their virulence may be experimentally increased or lessened. But if we inquire more minutely as to the external conditions necessary for the development of the infectious forms, there appears a breach in our knowledge which even bacteriology cannot fill up. This gap can only be bridged over temporarily by the so-called predisposition of time and place, concerning which we shall speak more fully later on. Now we wish to take up the important question as to how the bacilli, after they have become infectious, obtain entrance to the intestinal canal of a healthy individual.

PATHS OF INFECTION.

It has always been considered that there are two ways by which infection might take place—namely, through the respiratory organs with the air, and through the stomach with food and drink. The adherents of the strictly localistic school, especially von Pettenkofer and his followers, deny all infection through drinking-water; there remains, therefore, for them no way but infection through the air. The adherents of the more strictly contagionist school, whose chief leader is R. Koch, wish exclusively to consider the possibility of infection through food and drink, and to look on any other path of infection as an exception, brought about by the evaporation of fluids that

contain bacilli, so that the bacilli remain in the form of dust, or in some similar manner. My opinion is that both these schools see the question from a one-sided point of view, and that only a combination of both corresponds to the epidemiologic facts, which show with certainty that infection can and does frequently occur in both ways.

INFECTION THROUGH THE AIR.

For a long time it was popularly believed that cholera was conveyed through the air, like many other infectious diseases. It was considered that the virus was introduced through the respiratory apparatus in the form of dust. But the investigations of R. Koch, which showed that the ordinary comma bacilli were quickly killed by drying, brought this kind of infection into doubt, and recently many investigators have come to the conclusion with Koch that the introduction of the disease by means of the air is not at all, or only under quite uncommon conditions, possible. Yet such doubts are justified only so long as we refuse to assume that the bacillus can develop a more resisting form outside the human body. As a matter of fact, later investigations have shown that under proper conditions the ordinary comma bacillus is able to withstand drying for several days (Berckholtz, Kitasato), and that, especially when the bacilli are dried with clay, sand, or sweepings, they may be dispersed as dust in a living condition (Uffelmann). Even in feces they have proved themselves capable of living a much longer time than was before considered possible (Schiller, Abel and Claussen, Kaolinski, and others). There is, therefore, no theoretic consideration to prevent us assuming that the disease may spread through the drying and conversion into dust of the microbes. Under these circumstances, if taken up with the air in respiration, they could easily reach the intestinal canal. It has been thought that then they obtained entrance to the intestinal canal from the lungs by the circulation, but it is more likely that they lodge, like other dust, in the nostrils or pharynx and are later swallowed.

Epidemics are not rare in which the cases are so grouped that they seem to have arisen from a single focus. In such cases only the air is to be blamed for the transference. For the growth of such a focus of infection, it is necessary that the bacilli from a patient find a culture-ground suitable to their development into an infectious form. If they then dry up and become dust, numbers may be infected from such a focus of infection. Yet their striking distance in the atmosphere is undoubtedly only within a very limited radius.

These foci of infection may arise in any place where organic matter is present in a moist condition, as in drains, sewers, dirty dwellings, patients' bed or body-linen soiled with evacuations, and especially in water-closets and their soil pipes, in which ascending air currents often develop. A visit to an infected house, and particularly to an infected water-closet, is full of danger.

This mode of conveyance is especially to be thought of whenever infection has occurred independently of the water-supply; whenever isolated houses, or series of houses, are attacked; or, if in a given house, after one case, the majority of the inmates become sick while neighboring houses remain free from the pest. These house epidemics are similar to the ship epidemics which occur on the Indian Ocean on coolie vessels and pilgrim transports, but which were also seen in 1893 to a shocking extent on the Italian emigrant ships (Pfuhl).

Undoubtedly, too, in these cases the miserably arranged latrines (after the Italian fashion) were at fault.

Whether the disease can be spread by means of articles of commerce has not yet been absolutely determined. Isolated experiences seem to indicate that it is so spread, and the possibility of its spread through many articles that come in contact with the evacuations of patients cannot be denied. Second-hand clothes, scraps, and rags especially are to be regarded with suspicion.

At a short distance from a focus of infection the microbes dispersed through the air appear to be too scattered to still possess much infecting power. But that their power is not entirely worn out is perhaps best seen from the fact that during an epidemic a great number of people, though not specifically ill, yet suffer from a certain constitutional disturbance, and especially a tendency to diarrhea; though undoubtedly in many such people the disturbances are purely psychic.

[It is more than questionable whether cholera is conveyed through the air even in the form of infective dust. "The cholera bacillus is so readily killed by desiccation that such a mode of transference is in the highest degree unlikely" (Ernest Hart and S. C. Smith in Clifford Allbutt's "System of Medicine," 1896).]

INFECTION THROUGH THE DRINKING-WATER.

That the spread of cholera is due in many cases to the drinking-water has for a long time been recognized by the majority of observers. The epidemics and isolated cases which have been referred to it are numerous. It must be granted that the old observations were so incomplete that many epidemics have been attributed to this medium

for which other means of conveyance cannot with certainty be excluded. Yet there are still so many undoubted instances that it requires the extravagant skepticism of a von Pettenkofer to doubt its possibility. The experience of 1892, especially the great Hamburg epidemic, not to mention innumerable other observations, have made it impossible to exclude drinking-water as a means of infection.

It must be admitted that, in most cases where the behavior of the epidemic pointed to infection through the drinking-water, the presence of the bacilli could not be proved in it. Ordinarily, the cholera bacilli die quickly in absolutely pure water, and in impure, non-sterilized water they are soon overgrown by other micro-organisms. Still, it is possible that a more stable form might be able to live longer in water. And, as a matter of fact, recent investigations show that under special circumstances the cholera bacilli may remain alive and even develop for weeks and months in water. That, however, it is extremely difficult to prove their presence in water, and that the demonstration is only seldom successful, is easily understood if we reflect that, when present, they are widely dispersed in water, and are in the midst of numerous other micro-organisms which easily overgrow them on cultures. Moreover, among these other micro-organisms are many so similar in their behavior to cholera bacilli that they are differentiated from the latter with difficulty. Repeatedly comma bacilli which corresponded in most respects to the true cholera bacilli have been cultivated from still and running water; as from the Elbe at Hamburg, the Spree, the Berlin pipe-water, the Danube canal at Vienna, and the Seine at Paris. No single characteristic has been found which in all cases will differentiate these pseudo-forms from the true cholera bacilli; therefore all their biologic characteristics, even their virulence, must be taken into consideration (see under Diagnosis). There is even some question as to whether some of the microbes which are present in water, even if they show themselves but feebly pathogenic, may not be descendants of true cholera bacilli which, as a result of their long development on unfavorable media, have degenerated and lost some of their virulence. With such uncertainty in differentiation the greatest care must be exercised in judging of the results of water examination.

Yet in a few cases true cholera bacilli have been found in water. As far back as 1884, R. Koch found in a tank in Calcutta cholera bacilli with all their characteristic attributes. This tank furnished drinking-water and household water for the surrounding inhabitants at large, but it also took up the entire refuse of the houses, and in it the

linen from the first patient who died there of cholera was washed.
During the epidemics of 1892 and 1893, other investigators likewise
succeeded in cultivating cholera bacilli from still and running water
(C. Fränkel, van Ermengem, Biernacki, Lubarsch, Löffler, B. Fischer,
R. Koch, and others).   The most complete proof of the presence of
cholera bacilli in water was furnished at the time of the epidemic in
Nietleben, when they were found in the sewage as well as in the house-
hold water pumped from the Saal at the various stages of its baneful
course.

Contamination of water may take place in many ways.   In
navigable rivers it may result from ships and boats which, even with
cases of cholera aboard, dump their sewage directly into them.
Moreover, the water-courses are contaminated by the surrounding
inhabitants and by the sewers and drains which open into them.
Where drinking-water is taken direct from a river, or where the supply-
pipes are fed from a river, many may simultaneously be attacked
by cholera.   Perfect filtration gives protection, but filtration plants
frequently get out of order, with the result that some of the water
goes through unfiltered.   How far away from the site of contamina-
tion the water may be still infectious has not been determined, though
the Nietleben epidemic showed it to be no short distance.   These
cases of water contamination are the only examples so far of the
spread of cholera apart from the medium of travel.

Springs may also be contaminated if the microbes obtain entrance
through any supply stream.   The same holds, too, for ordinary
pumps and draw wells, if they are so situated that slop-water, or the
liquid from cesspools and dung-heaps, or the dirty water in which
a patient's linen has been washed, is allowed to flow direct into
them.   This frequently happens through an under-surface communi-
cation with water-closets and sewers.

In my article on the etiology of typhoid fever (von Ziemssen's " Hand-
buch," vol. II) I have detailed a series of ways by which typhoid may be
spread through the drinking-water. The same may also be applied to
cholera, though there is this striking difference, that the typhoid bacillus
possesses much greater resisting power and longevity than that of cholera.

If in a cholera epidemic a large number of people are attacked
simultaneously, the drinking-water should be looked to.   This so-
called "explosion form," in cholera as well as in typhoid, is character-
istic of a drinking-water epidemic.   The conjecture as to such an
origin becomes in the highest degree probable if only those are attacked
who draw their water from a special source, while all others, at least

in the beginning, remain exempt. Immediately following such an outbreak, however, foci usually form from which infection takes place in other ways, and from this time the number of cases originating independently of the drinking-water increases.

There are papers on the Hamburg cholera epidemic of 1892 from Reincke, R. Koch, Hueppe, Gaffky, Deneke, and many others. A very carefully compiled report, with many illustrations and charts, is that of the Royal Cholera Commission, prepared by Gaffky (1894), with the co-operation of several Hamburg scientists.

That the drinking-water played a principal part in the Hamburg epidemic is evidenced by its explosion-like appearance and its rapid spread through all parts of the city. The first case occurred on August 16th. Within the next few days the disease spread so rapidly that on August 27th the number of fresh cases was more than 1000. The first cases appeared in the neighborhood of the harbor, but the disease spread so quickly over the whole city that on August 21st the majority of the remaining districts were attacked, and on August 23d none were free from the disease. Ten thousand cases in all, with more than 4300 deaths, took place up to September 3d, when the epidemic began to gradually abate. From October 22d only isolated cases were seen, and after November 12th the disease ceased altogether. In the beginning of December there arose a small after-epidemic, which continued throughout the winter.

The water-supply of Hamburg was unfiltered river-water taken from the Elbe at a point above the city which, on account of the low water-level, the sewage of the city could reach at high tide, and above which many ships lay at anchor. Granting the presence of cholera, the opportunities for contamination of the water were innumerable. On account of the existing high temperature and low water-level, the water contained much organic and inorganic material, which made it especially suitable for the development, and perhaps the increase also, of micro-organisms. The water was delivered to the houses in casks, in which much organic matter was permitted to collect, thus multiplying the extremely favorable breeding places for bacteria. That the disease, as a matter of fact, was spread through the agency of the water is evidenced by the circumstance that it limited itself at first to the area of this water-supply, and that those only sickened who drank the water directly from the Elbe. Moreover, though Hamburg and Altona are close enough together to make one city, the latter, furnished with well-filtered water from the Elbe, escaped, at least at the beginning of the epidemic, if no account is taken of a few cases introduced from Hamburg. The same is true for Wandsbeck, which takes its drinking-water from a spring. The area of spread of the epidemic in Hamburg corresponded exactly to its water-supply. In the same street, those who used this water were attacked; others, who took their water from Altona, escaped. Institutions with numerous inmates, excluded from ordinary communication, but using the Hamburg water, suffered severely, while others, among them the barracks, with a different water-supply, were passed over, though cholera raged all around them. "We had here a sort of an experiment affecting more than 100,000 people, yet in spite of its huge dimensions, it fulfilled all the conditions that we look for in an exact laboratory experiment" (R. Koch). The after-epidemic in the autumn of 1893 is also to be referred to the Elbe water, and at

this time microbes were found in it that could not be differentiated from cholera bacilli.

The proof is absolute that the cholera epidemic of 1893 in the lunatic asylum of Nietleben, near Halle, was due to the drinking-water. We have complete reports on this epidemic from R. Koch, who was on the spot and made investigations at the time, and from Fries, the director of the institution. Since at the time there was no cholera in the neighborhood, and the season was not one favorable to its spread, the epidemic came as a complete surprise, without giving opportunity for preparation.

The first case was on January 14th. Six followed on January 15th and 11 on January 16th. Altogether, up to February 13th, 122 were attacked, with 52 deaths. The cases were distributed throughout the different wards and buildings without distinction. The institution derived its water from the Saal, and its filtration apparatus was so imperfect as to allow most of the water to pass through unfiltered. The sewage of the asylum was carried through the drain to a sewage farm, whence, the ground being frozen, it flowed off along the surface or through fissures, without undergoing any purification worth speaking of, to the so-called hog-ditch (Saugraben), and thence to the Saal. Cholera bacilli were found in the dirty water at its entrance to the sewage farm, in the sewage farm itself, and in the water leaving this by the main drain. Further, they were present in the hog-ditch, in the Saal near the opening of the hog-ditch, in the filtered water of filter No. II, and in the water from a delivery cock in the institution. With the cutting-off of the water-supply the epidemic ceased. Almost simultaneously with this epidemic, a series of towns on the Saal below Nietleben reported cholera in persons who, it was afterward proved, had drunk water from the Saal.

Yet even in these cases, when there is no doubt, as in the Hamburg outbreak, that the epidemic owes its origin to the water-supply, there is one point that remains unsolved—namely, whence came the first case by which the water became contaminated. Probably in the Hamburg epidemic the disease was introduced by personal attendants.

A very instructive example of a small epidemic originating from a single spring in Altona is described by R. Koch (1893).

OTHER MODES OF INFECTION.

Contaminated water, even when not drunk, but only employed for washing table utensils, may be a source of danger. In rare cases the accidental swallowing of water while bathing may bring about infection. It is to be remembered that the bacilli may live for a long time in ice. Milk, also, may act as the medium of infection, if the vessels containing it are washed in contaminated water, or if it is diluted with the same.

Under special circumstances the bacilli may enter the intestinal canal in food, if this has been directly contaminated or exposed where the bacilli from the air may fall on it. In the Institute of the Imperial Board of Health and in other places extensive series of experiments have been carried out to determine the behavior of cholera bacilli on the surface and within the substance of fresh fruit and of

different foods and drinks (Kitasato, Heim, A. Friedrich, and others). It was proved that under certain circumstances the bacilli remained alive long enough to make infection by these means possible, and there are isolated examples in which the disease was very probably so acquired. Though such cases must be rare in comparison with other means of infection, they are especially important since they furnish a method of introduction to a place to which no sick traveler has come.

The possibility of the spread of the microbes by flies and other insects has been repeatedly suggested (R. Koch and others), and direct experiments have proved that it may occur (Simmonds, Uffelmann, and others).

DURATION OF LIFE OF THE CHOLERA BACILLUS.

Of great importance is the question how long the cholera microbe can live and remain effective outside the human body. Experience seems to show that in our climate it usually dies soon unless revivified from time to time by passing through a human body. As a rule, if three or four weeks have elapsed without new cases appearing, we may conclude that no more effective bacilli are present. A new epidemic can then result only after a fresh introduction of the disease.

Yet there are exceptions to this; for it has happened that, many months after an epidemic had apparently ceased, it appeared again in the same place without a fresh importation. Sometimes exact investigation shows that, in the apparent interval, isolated, mild, and consequently but little heeded, cases occurred; but in other instances again, no such explanation is forthcoming, and the organism appears to have remained effective an uncommonly long time outside the human body. Moreover, the fact that cultures of the bacilli may be transplanted in nutritive media for an unlimited time certainly suggests the possibility under especially favorable conditions of the organisms living a long time in the ground or in other places.

This does not exclude the fact that the virulence decreases or is even lost with time, because by changing the medium or temperature this can be increased. In the soiled linen or bedding of cholera patients, if they are kept packed in a moist condition, the bacilli remain effective for a very long time, so that the handling of these articles is extremely dangerous.

In the parts of India where cholera is endemic it seems never to cease. The following statistics from Schumburg represent the steady continuance

and spread of the disease in India. It will be noticed that it has increased in recent years. There have died in India of cholera in the years:

1880	119,256	1886	208,371
1881	161,712	1887	488,788
1882	350,971	1888	207,408
1883	248,860	1889	428,923
1884	287,600	1890	297,443
1885	385,928	1891	601,603
	1892	721,938	

For the last year (1892) the records of 5 provinces are wanting.

PREDISPOSITION AND IMMUNITY.

A cholera epidemic can arise in a place only after the introduction of the bacilli. Yet the bacilli may be carried there and no epidemic ensue. If a person comes to a hitherto non-infected place with cholera bacilli in his intestine, the chances are that they will spread no further, or, if they do, it will be at most to a few persons in his immediate neighborhood. In recent years this can be explained by the fact that strangers arriving indisposed are closely watched and their evacuations are rendered innocuous; but even before our day, when no precautions were taken, the same held true.

There is no doubt that by far the greatest number of bacilli thrown off by a cholera patient become innocuous for other people. Many die at once because they find no suitable medium, or for want of moisture, or because they are mixed with substances injurious to them, or are overgrown in the struggle with other micro-organisms. Others live a longer or shorter time, and possibly even multiply, but they are not capable of infection, because the conditions are wanting that go to produce the necessary resisting power and virulence. Finally, others that are perhaps effective fail to find susceptible subjects.

Von Pettenkofer and all those who support the theory of predisposition of locality are certainly correct when they affirm that the presence of cholera bacilli in a place is not sufficient to call forth an epidemic, but a series of local conditions are required besides. What these conditions are, von Pettenkofer's school has not told us, and our own knowledge of the biology of the organism does not suffice to enable us to trace them. Yet observation of the epidemiologic behavior of cholera has shown us a number of principles that are in part theoretically intelligible.

Whether or not an epidemic follows the introduction of the disease depends oftentimes on accident, in the same sense that it is accidental

whether the single isolated grain of wheat falls on good ground and grows, or on a rock and dries up, or is eaten by the birds. In many cases the circumstances are so trifling as to be overlooked, or allowed to pass without their significance being understood. Many other conditions, further, have been determined by experience, and their significance can be calculated.

All the circumstances that favor the rise of an epidemic, or that increase the susceptibility of the individual, are commonly called auxiliary [or predisposing] causes (Griesinger). But it would perhaps be more exact to avoid the word "cause," for all these auxiliary causes taken together would not make an effective cause: they could never produce cholera if the peculiar and specific cause, the cholera bacillus, was absent. Conforming, then, to this idea, we will speak of a local predisposition in relation to epidemics, and of an individual predisposition in relation to the origin of the disease in individuals. With a change in the conditions, both these may change in the course of time, and in this sense we will speak of a predisposition of time or season.

Moreover, where the conditions are unfavorable to the origin of an epidemic we will ascribe to the place a permanent or temporary immunity against the disease.

PREDISPOSITION OF LOCALITY.

The local predisposition of many dwelling-places, or even of different parts of cities, is shown by the fact that in almost every epidemic they are the first to be attacked or suffer most severely. Other places, on the contrary, exhibit a certain immunity, inasmuch as, even after the introduction of the disease, usually no epidemic arises. We may mention as more or less immune, for example, the cities of Stuttgart, Würzburg, Darmstadt, Frankfurt a. m., Freiburg in Saxony, Salzburg, Innsbruck, Bozen, Lyons, Versailles, and Birmingham. No place is, of course, absolutely secure from cholera, and many towns and regions that considered themselves immune, because earlier epidemics passed over them, have been severely attacked by later ones.

Würtemburg was repeatedly skipped in the earlier pandemics of cholera. This may have been due partly to the fact that it was out of the line of travel, and consequently the introduction of the disease was difficult. Yet, even when the disease was introduced, no very great epidemic followed. In the same way, for instance, the disease was repeatedly carried into Stuttgart without ever causing an epidemic.

Cholera made its first appearance in different parts of that capital in 1849. In one place 21 died, in another 10, in a third 6. In all others it

spread so little that the number of deaths in any given place did not exceed 4. In that whole year, in all only 52 died of cholera. In the summer of 1854 cholera appeared in 27 places in Würtemburg; yet the total mortality was only 127. In the summer of 1866, though during the war cholera was present in the neighboring Grand Duchy of Baden, only a small epidemic with 18 deaths occurred in Würtemburg. It seemed possible, therefore, to assume that in Würtemburg there was no culture-ground for the disease.

In 1849 a case was introduced into Heilbronn without further result. But suddenly and unexpectedly in August, 1873, without any proof that cholera had been introduced into Heilbronn, though it was at the time prevailing in northern Germany, Vienna, Munich, and Würzburg, there broke out in Heilbronn an epidemic in which, within two months, 192 persons were attacked and 62 died. Of those attacked, 161 were taken ill in the first 4 weeks. From Heilbronn the disease spread to the neighboring towns, though in the most of these the number of cases was small. In only one, Frankenbach, a village at one hour's distance, did there appear a real epidemic, with 34 attacks and 20 deaths.

This Heilbronn epidemic has been reported by Höring and von Holz. The lesson to be learned from it is that even in Würtemburg it is not safe to trust to the previous immunity, but every prophylactic measure must be taken by which an epidemic can be prevented or limited.

The cholera epidemics in Würtemburg in earlier years have been described by Keyler, Riecke, Köstlin, Elsässer, Veiel, Schäffer, Teuffel, and Burkart.

The examples are numerous of places which early experiences proved immune, but which have been occasionally severely attacked. As, for instance, the summer residence of the Czar, Peterhof, near St. Petersburg, which as a result of careful quarantine remained free in 1831, and was also spared during the epidemics of 1866, and from 1870 to 1872. In 1848 and 1854, however, it was severely attacked, so severely that on the former occasion 2.16% and on the latter occasion 1.6% of the population suffered (Dobroslawin). Even Lyons, considered so pre-eminently immune, had a cholera epidemic in 1854.

The predisposition of a place is especially great where masses of decomposing material lie about. Overfilled latrines, manure-heaps, poorly flushed sewers, dirt and uncleanliness of all kinds, both above and below ground, effect favorably the spread of an epidemic. The manner of disposal of the drainage and sewage exercises a great influence. In many towns and districts where cholera had been in past years frequent and severe, the local predisposition has been considerably lessened by a thorough sewerage system, and an improvement in outhouses. A loose and porous soil, rich in decomposing matter from outhouses and sewers, is calculated to become a breeding-place of the disease. Consequently places that lie above alluvial, diluvial, and tertiary formations are comparatively more frequently and severely attacked; while others that lie above compact rock often exhibit a relative immunity.

A moist subsoil, and especially a trough-shaped surface that allows no free out-flow of water, is in general necessary for the spread of the disease. Yet there are places standing under water, to which access of air is thereby prevented, such as marshes, that show only a slight predisposition. A marked fall in the ground-water after a previous high level seems to increase the predisposition, partly perhaps because extensive tracts are left open to the air in a moist condition, but especially because, as I have shown in 1886 in the etiology of typhoid fever, the possibility of bacilli gaining entrance to the drinking-water becomes greater. Yet so far the influence of the changes in the ground-water is by no means as evident for cholera as it was for typhoid fever in Munich.

The relative height of a place is also of importance. As a rule, high situations are less frequently attacked than valleys; and in cities, the higher districts less than the lower ones. Frequently the disease spreads by preference along a river bank, and this has been noticed as occurring independently of traffic and the use of the river-water. In cities the thickly built and densely populated parts usually suffer most. Likewise almshouses, foundling-houses, prisons, lunatic asylums, and indifferently managed hospitals are dangerous.

For most places and most institutions, the thing of greatest importance is the water-supply. Where the drinking-water is not absolutely protected from contamination and drainage or sewage, the possibility is always present, after the introduction of the disease, that a frightful epidemic may suddenly break out.

PREDISPOSITION OF TIME.

In the predisposition of time, season occupies the most prominent place. In temperate climes epidemics usually begin in summer, reach their acme in August or September, and then decline. As a rule, the epidemic ceases with the setting-in of continuous frost. So striking a dependence on the external temperature would be incomprehensible in a purely contagious disease, and, needless to say, it does not occur in smallpox, measles, scarlet fever, and typhus, which show a predilection for the winter months, but only because people are then huddled closer together in houses. The existence of such a dependence in cholera shows in an unmistakable way that the exciting cause of the disease, like that of tyhpoid fever, requires for its growth and development certain conditions not only in the external world, but also in the human body. Moreover, in large cities we sometimes see a continuance of the disease throughout a winter in

isolated cases, while later on, with the appearance of warm weather,
it again acquires a wider distribution.   Occasionally, too, winter epi-
demics have been observed.   These appear especially in northern
countries (St. Petersburg, Moscow, Bergen in Norway), and are
undoubtedly partly due to the circumstance that then the heating
extends over the whole house, even to the water-closets.

The dependence of cholera on the season is shown in an indisputable
manner by the investigation of A. Hirsch (1881), based on 920 epidemics
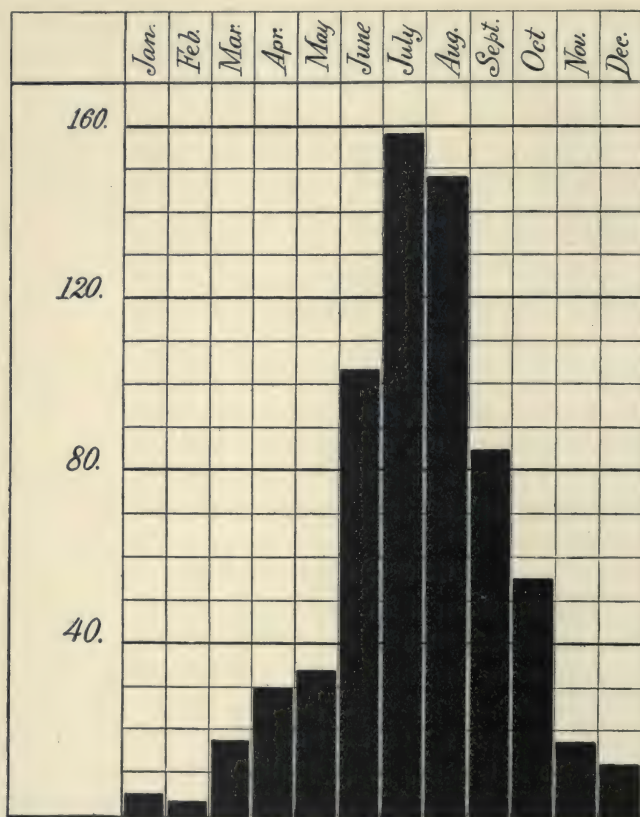
Fig. 10.

outside of India, with reference to the time of their appearance and espe-
cially their predominance.   Of these 920 epidemics, 647, or 70%, took
place in the four months June to September inclusive.   If we omit those in
regions where the mean temperature for the year does not exceed 15° C.,
we have 668 epidemics; 495, or 74%, of which fell in the same four months.
Figure 10 gives a graphic representation of these epidemics in the separate
months.

A similar condition is found when we compare the number of deaths from cholera that take place in different months in any one country. Figure 11 shows the number of deaths from cholera in England in 1849; figure 12 gives the sum of the deaths in separate months for the three years 1853 to 1855 in Russia.
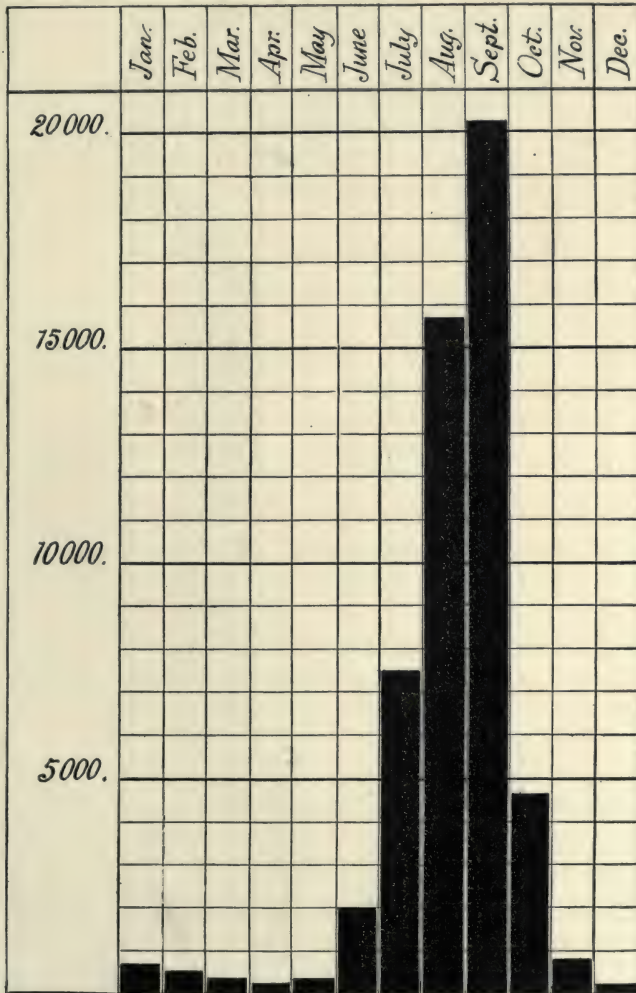
Fig. 11.

It can easily be understood that such a dependence on season is less evident in tropic and subtropic countries. In Calcutta, for example, the acme of cholera falls in the months of March and April, and in general it is more frequent from November to May, the months which show the lowest temperature, but the greatest dryness. In Bombay cholera is most

frequent from January to June.   In the North-West Provinces of India the
months June to September are the worst.

Weather has but an indirect influence, acting only so far as the
temperature of the air and ground, the moisture of the latter, and
other factors are dependent on it.   Thus it is evident that like changes
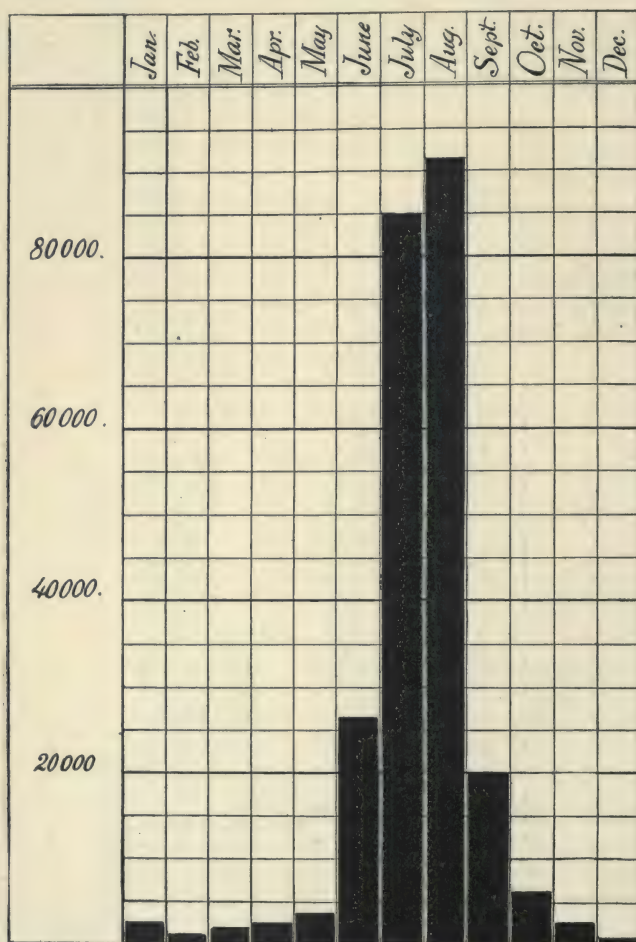
Fig. 12.

of weather may have quite different effects in different places.   A
heavy rainfall in dry regions with a porous soil may increase the
predisposition, while the same in damp places, by putting an exten-
sive surface under water, and perhaps washing away the filth, may

lessen it. Likewise, when there has been a previous drought, through the setting-in of wet weather, a better drinking-water will become available.

Atmospheric electricity, fluctuations in the magnetic force of the earth, the quantity of ozone in the air, barometric oscillations, etc., are said to have an influence, but this influence cannot be recognized from the facts.

Since the disease is spread by traffic, it is clear that the assembling of large crowds for pilgrimages, exhibitions, fairs, annual markets, public festivals, etc., may bring about an epidemic. And it has frequently happened under these circumstances that the appearance of the disease dispersed the crowd in all directions, with the result that the disease also became wide-spread. In India, from time to time, religious bathing festivals are celebrated, to which immense numbers, 100,000 souls or more, gather. These bathe in the Ganges and drink from the holy stream. These masses coming from the most distant parts are the cause of the most wide-spread epidemics. The most serious danger for Europe since the opening of the Suez Canal lies in the pilgrimages of the Mohammedans to Mecca. Cholera is brought to this place by pilgrims from India, who die of it in vast numbers. Thence it is carried by others to Egypt, whence by ship-traffic to Mediterranean ports it reaches Europe. Also, as has been mentioned, the old epidemic route through Afghanistan and Persia to Russia was taken by it again in 1892. The concentration of troops and their marches favor in a high degree the origin and spread of cholera. Moreover, during war if it breaks out in one camp, it is common to see it run through both armies, and usually with a dreadful mortality.

Of vital importance in the spread of an epidemic is the conduct of the medical profession and of the authorities in relation to the first cases. When these are recognized early and all preventive measures taken, an epidemic can usually be avoided. The experience in Germany in this regard since 1892 is especially gratifying. Although isolated cases have been widely spread, in but few instances has an epidemic arisen.

INDIVIDUAL PREDISPOSITION.

To the question, Why, in an infected region, do some take the disease, and others (and those usually the majority) not take it? we must answer that it is due in great part to accident. It is the same question, Why does the bullet strike one and miss another?

Yet this is not all. There are undoubtedly circumstances that make one individual more liable to it than another. We can name some circumstances which are of more or less importance, the significance of which can in part be theoretically understood.

First may be mentioned many individual inclinations and habits which favor or hinder the taking of the disease. Uncleanliness of every kind favors it; for example, the habit of eating without washing the hands, or of drinking every sort of water indiscriminately. The frequent washings prescribed to Mohammedans would militate against infection, if, unfortunately, they did not counteract the effect by drinking the water in which they washed. The frequent occurrence of the disease on river boats and among dock-laborers is not seldom due to the drinking of water contaminated by the evacuations of both the healthy and the sick. That the poorer classes are attacked in proportionately larger numbers is attributable to the greater opportunities for infection brought about by their conditions and occupations; for instance, washerwomen who come in contact with the linen of cholera patients. Particular trades may, on the contrary, carry with them a certain amount of immunity, as, for instance, the brewery business; though in this case it is doubtless partly the result of the laborers being accustomed not to drink water. The immunity of workers in tobacco and of tanners may possibly be referred to the disinfecting effect of the tobacco and of the tan-bark.

Yet these differences in opportunity for infection are not sufficient to explain all the differences in the susceptibility of the individual to the disease. There is also an individual predisposition in a narrower sense: that is, even if the cholera micro-organisms are actually inoculated, one person will not be affected, while another will be severely attacked. Living cholera bacilli have been repeatedly found in the stools of healthy people who exhibited no symptom of the disease. And, further, the severity of the disease is in no way dependent on the number of bacilli which may be present. There remains, then, only this, that one person is more susceptible, another more immune. The causes of this difference have been so far only conjectural. In certain cases a question as to the less or greater virulence of the microbes might arise, or, again, the presence in the intestine of particular bacteria that are inimical to cholera bacilli. Further, the gastric juice is of importance, since when normal it can render at least the ordinary cholera bacilli innocuous. An anatomically and functionally normal intestinal epithelium may also give a certain amount of protection.

Generally speaking, it is à *priori* probable that a healthy strong man with functions normal would have greater resisting power than an enfeebled or diseased one. As a matter of fact, it appears that every debilitating influence increases the susceptibility. The disease therefore preferably attacks the lower classes, not only because they are more exposed to infection, but also because they labor under more injurious influences by which their resisting power is lessened. Especially frequently are those attacked who suffer from chronic or constitutional ailments, or are recovering from acute diseases, or are habitual drunkards. The circumstance which is sometimes observed, that the death-rate in a population among which the mortality has been markedly increased by a cholera epidemic falls below its average standard in subsequent years, so that if several years are taken together the influence of the cholera on the mortality almost disappears, is principally explained by the fact that the disease carries off many who would otherwise have been included in the mortality of the immediately succeeding years.

Cholera may occur simultaneously with other acute diseases, so that it has been observed to attack those ill of typhoid fever or laryngeal diphtheria. Usually in those cases both diseases run their courses independently and without interrupting each other, though the danger to the sick man is decidedly increased. On the occurrence of cholera in a typhoid case the splenic enlargement quickly disappears.

Among the occasional causes which develop the disease after the introduction of the microbes may be mentioned great exertion, deprivation, colds, gross dietetic errors, emetics, and purgatives or whatever causes diarrhea. That the increase of many epidemics is more marked on Monday and Tuesday than on other days of the week seems to be due to the greater frequency of dietetic errors on Sunday. Depressing emotions—among others, fear of the disease—may increase the susceptibility.

The disease seems to bring with it a certain degree of immunity, for a time at least; though it is not uncommon to see a person attacked in two succeeding epidemics. The attempts to produce an artificial immunity by inoculation of the products of the bacilli, or with the blood-serum of persons who have passed through the disease, have so far proved futile.

Sex and age have little influence, though old people are attacked more, infants less, frequently.

BEHAVIOR OF EPIDEMICS.

The number attacked in proportion to the number of inhabitants in a place differs extremely in different epidemics. In general, we may say that the percentage is usually lower in large cities than in small towns or villages.

In St. Petersburg in 1831, 2% of the population were attacked; in 1848, 2.7%. In Moscow the morbidity was in 1831, 2.5%; 1848, 2.2%. In Berlin the highest figure reached was 1.3% (1837 and 1849); in Vienna in 1836, 2.3%, against 0.5% in 1850; in Prague in 1832, 3.4%; in 1855, 1.6%; in Heilbronn in 1873, 1%. Higher figures were found in other places, as at Plymouth in 1832, 6%; and in 1848–49, 8%. In Messina in 1855, 22% of the population died.

In Hamburg in 1892, 2.7% were attacked; in Altona only a little over 0.4%.

In smaller communities and in villages it is not very unusual to see more than half the population suffer. In certain small towns in Austria in 1855 the morbidity reached 80%, and the mortality rose even to 43% (Drasche).

The duration of epidemics is likewise very different. On an average they last longer in large cities than in small places. In the very large cities epidemics scarcely ever run their course in less than three or four months, and when they last through the winter, outbreaks may continue for over a year. In smaller towns and villages they usually terminate in two or three weeks, and only rarely do they extend over several months.

In a cholera epidemic the greater the number attacked, the greater the opportunity of infection for the other inhabitants of the place; therefore, as was to be expected, the number of the attacked increases daily. As a matter of fact, the outbreak at first usually answers to this canon. But after a certain time, in small towns earlier, in large cities later, the acme is reached, when the number of daily attacks begins to grow less, and finally the epidemic ceases. This is true even on ships, where, under the worst conditions, the epidemic will not last more than a few weeks, provided the ship remains long enough at sea.

What is the cause of this gradual decrease and final cessation of the epidemic? This question can be only partly answered in the present state of our knowledge.

In many cases a change of season, especially the advent of a cold winter, will bring about this result; yet many epidemics come to an end without the possibility of ascribing a decisive influence to either weather or season. Again, the fact must be considered that in the

course of the epidemic many susceptible persons have been killed off, and others have passed through the disease; yet this consideration—which can explain, for instance, the cessation of an epidemic of measles—will not answer for cholera, since ordinarily only a small proportion of the inhabitants suffer, even up to the close of the outbreak. A great influence is in many instances exercised by the active measures adopted by the public health authorities, the care which individuals take at such a time, and, lastly, the flight also of a portion of the inhabitants. Still, all these conditions are insufficient, and it is in the highest degree probable that other circumstances must cooperate.

It is a fact observed in almost all large epidemics that after the acme has passed not only does the number of those attacked decrease, but also the mortality among these becomes less. The majority of cures recommended in cholera have become known on account of their effect on cases toward the end of an epidemic. It appears, therefore, that in the course of an epidemic the virulence of the bacillus gradually lessens, and it is likely that with this loss of virulence there is likewise a decrease in its vitality, and power of development. If we reflect that the cholera bacillus is an exotic growth, the supposition appears admissible that it may gradually lose its vitality through its prolonged evolution in the same place outside its native sphere; and this conjecture will explain the gradual termination of an epidemic. Moreover, as the individual who has had the disease is immune for a time, so a certain immunity, though of short duration, is conferred on a place contaminated by the organisms. Such a gradual decrease of vitality of the microbes outside their native sphere will likewise explain the striking phenomenon that the pandemics originating in India have so far never led to a lasting implantation of the disease in other lands, but on every occasion, after spreading for from eight to twelve years over all parts of the earth, it has disappeared, and for a time has been again limited to its place of origin. For a new outbreak in other countries there must be another transplantation of fully vigorous microbes from India.

PERIOD OF INCUBATION.

In cholera, as in other infectious diseases, a person becomes ill not immediately on the introduction of the microbe, but some time afterward. This period of incubation may be very different in individual cases. There are cases in which the disease broke out within twenty-four hours after exposure to infection, but there are others in which several days, in fact, even eight to fourteen days and more, elapsed.

In these latter it sometimes happened that there existed for some time a slight diarrhea which was neglected, until suddenly, possibly brought on by gross dietetic errors, severe symptoms appeared. In the great majority of cases the period of incubation is considerably shorter, and usually even shorter than in most other infectious diseases. An average of two or three days may be assumed, though if, as is theoretically more proper, the beginning of the disease be reckoned not from the severe symptoms, but from the prodromal diarrhea, a still shorter incubation must be measured.

Von Pettenkofer has grouped the cases from the epidemic in 1854 (see Hauptbericht), in which persons from a non-infected district went into an infected one and were there attacked; in 5 such cases the disease followed within two and one-half to five days after their arrival. In comparison with this, observations were made on persons who went from an infected to a hitherto non-infected place, where an inmate of the same house or a neighbor became sick. From the arrival of the infected person to the breaking-out of the disease in another, there was, in 18 cases, an average interval of seven to eight days. So far as can be judged from the small number of observations, there is a difference in the two groups of about four days, which may be taken as the average time necessary to the cholera bacillus to develop outside the human body into the infectious form. However, these figures make the average duration of the period of incubation too long, since it cannot be assumed that in every case the disease was acquired at the first opportunity.

SYMPTOMATOLOGY.

We reckon as cholera all diseases caused by the specific cholera microbe. These diseases exhibit marked differences, from the very mild cases in which the sufferers scarcely realize that they are ill to the severe ones which usually end in death. Between these lightest and most severe cases come all grades, and it frequently happens that an attack beginning in a mild form will later develop into a severe form. In the symptomatology we will consider first the frank, outspoken disease, and take up later the milder and less pronounced cases.

GENERAL DESCRIPTION.

The course of this disease is usually divided into 3 stages: A first stage is distinguished as that of the prodromal diarrhea, a second as the stage of the real cholera attack, and a third as the stage of asphyxia, or, in favorable cases, as that of reaction.

The prodromal diarrhea usually consists of liquid evacuations of normal color without pain or tenesmus. There is commonly gurgling in the bowels, sometimes loss of appetite, a feeling of discomfort, malaise and depression, and a tendency to a cold sensation in the hands and feet. Otherwise the general condition is not disturbed and any feeling of serious disease is wanting. Such diarrheal attacks are seen in many people at the time of a cholera epidemic without serious symptoms following. But in many instances this diarrhea passes over into a regular cholera attack after a duration of one to three days. This prodromal diarrhea may altogether fail to show itself, and the disease may be ushered in with violent choleraic symptoms.

The real cholera attack consists in a sudden aggravation of the diarrhea, sometimes the result of an adequate cause (as a purgative); again, without one. Profuse liquid evacuations succeed each other rapidly, usually without any pain or tenesmus. The fecal masses still show at first a normal yellow staining with bile, but they afterward become colorless and consist of a watery fluid filled with whitish-gray flocculi. These so-called "rice-water stools" are especially character- istic of the severe form of cholera. Vomiting sets in, sometimes simul- taneously with the increase in the diarrhea, often for the first time

later. The contents of the stomach are next vomited or whatever has been swallowed. Following this, there appears a vomit of matter resembling the rice-water stools. Sometimes a tormenting hiccup comes on.

A severe attack quickly effects a striking change in the condition and appearance of the patient. The skin, as a result of the loss of fluid, becomes shrunken, loose, flabby, and shriveled. If pinched up, the creases disappear slowly. The nose is pinched, the eyeballs are sunk in the sockets, the cheeks are hollow, the malar bones stand out, and often the face is so changed as to be unrecognizable (*facies cholerica*). The heart-beat, its tone, and the pulse become weaker; the extremities, the nose, and the ears become cold. A certain degree of cyanosis develops, in that the skin becomes dark gray, grayish-blue rings surround the eyes, and a bluish color appears on the lips, hands, and feet, and especially about the nails. All secretions except the exudation from the intestine cease or are decidedly lessened, the urine especially is entirely suppressed toward the end. There is intense thirst, which, on account of the failure of absorption in the intestine, cannot be quenched. Painful cramps appear, most frequently in the muscles of the calves, but also in those of the thighs, arms, abdomen, and in other muscle groups. · The reflexes are markedly lessened, and the only responses to irritation are sneezing, coughing, or the contraction of the ocular muscles. Even the pupils often react but slowly. The voice, as a result of the drying of the vocal cords and the weakening of the muscles of the larynx, becomes husky or mute (*vox cholerica*). The defective circulation in the lungs brings about disturbances of respiration, and often the feeling of want of air. Moreover, the carbon dioxid output has been repeatedly found to fall below normal. The patient feels extremely prostrated, and complains of the violent thirst, dizziness, and palpitation. Despite the coldness of the skin, he does not feel chilly; on the contrary, he complains of intolerable heat, and struggles against heavier bed-clothing. There is frequently a feeling of great pressure and anxiety, oftentimes localized in the epigastrium (precordial anxiety). Complete consciousness is retained, though there is often apathy as to surrounding events, and even as to his own condition. In general, the subjective feelings of illness are much less marked than would correspond to the severe objective symptoms.

In the most urgent cases the condition passes into the stage of asphyxia, which usually leads to death. In more favorable cases the stage of reaction appears.

The expression asphyxia, commonly but wrongly employed to indicate cessation of breathing, is in this case thoroughly appropriate, since it properly signifies failure of the pulse (ἀσφυξία in Galen, from σφυγμός, "pulse").

The asphyxial, algid, or paralytic (ataxic) stage (*stadium asphycticum, stadium algidum sive paralyticum*) is characterized by an extremely marked depression of the circulation. The heart action is faint and irregular; the first sound is feeble, the second is often quite inaudible; the radial pulse becomes weaker and weaker, and finally imperceptible. On cutting into the swollen veins a dark, thick blood makes its appearance, which does not brighten on exposure to the air. Later, it entirely fails to flow, and in the worst cases incision of an artery produces no hemorrhage. The skin is cool, often moist and cold, and sometimes is covered by a clammy perspiration. The peripheral parts of the body, especially the extremities and the face, become cold, approaching even the surrounding temperature. Respiration becomes difficult, the expired air cool. The skin is leaden-gray, cyanotic, with here and there, especially on the fingers, toes, and ears, dark violet or blackish-blue spots. The stools become smaller or cease altogether, because no more fluid can exude from the blood-vessels. The effects of the loss of water become more evident; there is complete aphonia; vesication or burning of the skin fails to raise a blister; the mucous membranes in contact with the air, as the lips and tongue, become dry; the lacrimal secretion disappears, and since the eyelids can no longer be completely closed, portions of the eye dry up, so that dark or cloudy spots appear on the conjunctiva, or opacities of the cornea form. The internal organs also suffer from the lack of moisture, so that, for instance, friction sounds may be heard over the pericardium and pleura. Râles are not heard over the lungs. Consciousness is still present, but is decidedly enfeebled. Intense thirst, precordial anxiety, and a feeling of oppression continue. Finally, death sets in, sometimes a few hours after the beginning of the attack, frequently in the course of the first, or at latest in the course of the second day. In rare cases it happens that the patient may recover, and enter on the stage of reaction.

Those patients in whom an asphyxial stage has not fully developed, or who have survived the stage of asphyxia, enter into the stage of reaction (*stadium restitutionis sive reactionis*). Vomiting ceases, the evacuations become less frequent and more consistent. They resume their yellow color. The heart action grows stronger, the temperature of the peripheral parts rises, the voice comes back, the precordial anxiety

disappears, the cyanosis vanishes, and the urinary secretion returns. There is still considerable weakness and prostration at first, but in not very severe cases perfect health is restored in a few days. In other cases convalescence is slower and shows intermissions. The heart action remains weak and changeable, the temperature of the periphery rises slowly and irregularly, the secretion of urine continues scanty and it contains much albumin; sometimes marked feebleness of the heart and asphyxia set in, or there may be a regular relapse with renewed profuse diarrhea and the other symptoms. In many cases during the stage of reaction fever comes on (reaction fever), and continues for one to several days, accompanied by a rapid and dicrotic pulse, headache, and even by somnolence and delirium. Finally, in not a few cases, convalescence is disturbed by complications and sequelæ that often even endanger life.

Numerous patients after severe attacks, especially if they have passed through the stage of asphyxia, exhibit after-symptoms of a cholera-typhoid. Under this name are included many conditions all of which have in common the so-called "typhoid state" or marked benumbing of the sensorium. We shall discuss these conditions with the complications and sequelæ.

EXPLANATION OF THE SYMPTOMS. PATHOGENESIS.

It is the province of pathogenesis to show how the symptoms which come under observation in cholera proceed from the presence and development of the specific microbe of that disease. This investigation is not alone of theoretic interest, but has a wide practical significance, in that a clear conception of the pathogenesis can lead us to recognize the points to be assailed with an effective treatment.

The first question that arises is whether in cholera the microbes are present only in the intestines and affect directly these alone, or whether they gain entrance to the blood, and so affect directly all organs. In other words, Is cholera to be considered among the local or general infectious diseases?

From time immemorial local and general diseases have been differentiated. In the former the causal factor affects directly only one or a few parts of the body; in the latter it is spread throughout the body and may act directly on all organs. Still, it must be remembered that a local disease may indirectly cause general disturbances, and that many general diseases are characterized by their local lesions. With this reservation, the distinction in question remains good, and is quite necessary for the understanding of the pathogenesis.

Many physicians consider it self-evident that an infectious disease

must be a general disease, and this view is responsible for many a misinter-pretation in pathology. There is assuredly nothing in the conception of infection that would denote a general disease. True, many infections are general diseases, as smallpox, measles, scarlet fever, typhus, typhoid, influenza. In these the specific exciting cause is in the blood, and can therefore reach and directly affect all organs. On the other hand, there are other infections which are quite local, as gonorrhea, and simple, non-syphilitic chancre. Finally, other diseases are at first local, but may become general if the micro-organism gains entrance to the blood; the best example of this is tuberculosis, which is commonly local, but after the bacilli are disseminated by the blood becomes (as a diffuse miliary tuberculosis) a general disease.

It cannot be doubted that cholera belongs to the local infectious diseases, in that the specific micro-organism directly affects only the intestinal canal. This produces there what may be designated as an especially severe catarrh of the intestinal mucous membrane. This view was often put forward long ago, and in particular F. Niemeier (1849, 1861) based his investigations upon it, but it received little recognition, in great measure because may physicians had no conception whatever of a local infectious disease. As a consequence, earlier investigators usually sought for the causal micro-organism, not only in the intestine, but also in the blood and other organs, and it came as a surprise to many when R. Koch discovered the specific microbe only in the intestine, but not in the blood or other organs. Further investigations confirmed this discovery, and likewise the local nature of the infection. It is true that the specific bacilli have been occasionally found in the blood and other organs, but these findings are very exceptional, and the fact remains that as a rule, and in the great majority of cases, cholera bacilli are present only in the intestine.

The present more or less wide-spread opinion that cholera is a general disease is based on the fact that many organs exhibit severe disturbances which can be explained only by a participation of these organs. The local effect of the microbes on the intestinal canal is sufficient to explain the intestinal symptoms, such as the copious exudations, the violent diarrhea, the vomiting. But how are we to account for the heart failure, the cyanosis, the shriveling of the skin and subcutaneous tissue, the muscular cramps, the nephritis, the symptoms of cholera typhoid, and the other general symptoms? To explain these, must we not assume a direct action of the micro-organism on the blood, heart, nervous system, and other organs? We can answer this question in the negative. These disturbances are not dependent on a direct action of the microbes on the different organs, but are to be explained as the indirect effect of the process in the intestine.

An effect of the process in the intestinal canal on the rest of the body may be brought about either through the blood or through the nerves. In reference to the former must be considered the loss of water from the blood and tissues as a result of the profuse exudations, in addition to the absorption of metabolic products of the bacilli that act as a poison to the body. By way of the nerves the severe disease of the intestinal mucous membrane, like other severe and wide-spread irritations or wounds of organs, may cause further disturbances, and especially heart-failure. Many physicians have looked more or less exclusively to one or other of these three considerations for the explanation of all the phenomena, but, according to my opinion, all three are necessary. Depending on the individual case, sometimes one, sometimes another of these is the most important, although, again, it may not be possible in every individual case to distinguish the effects of these different factors from one another. [It is, however, quite certain that for an adequate explanation of the phenomena all three factors must be taken into account.]

The loss of water in the body as a result of the profuse exudation into the intestine was long ago put forward as a cause for the general symptoms, but recently this circumstance has been estimated at, I think, too low a value. The enormous amount of water poured out into the intestine in a short time in severe cases is at first drawn from the blood. Such a subtraction from the blood is possible only when it is immediately replaced, in part at least, by the reabsorption of water from all the tissues. But even so, a thickening of the blood is brought about, while all the tissues suffer from a want of water. Under these circumstances dropsical effusions are quickly reabsorbed, and even inflammatory exudations in the pleura and other body cavities have been seen to disappear in the course of an attack of cholera.

By the loss of water from the tissues, in the next place, are explained the decrease in swellings in all parts of the body, the sinking in and shriveling of the skin, the drying-up of the mucous and serous membranes, the soundless voice, the arrest of secretions, the violent thirst. The cramps in the calves of the legs and in other muscles may also be referred to the want of water in the muscles and nerves, since they are felt in other conditions associated with a marked loss of water.

Almost two-thirds of the body-weight of man consists of water; whilst, however, man and the higher vertebrates also will lose very nearly all of the body-fat and well-nigh half of the body-albumin before they die of starvation, they are much more sensitive to loss of water. Rubner assumes that not 10% of the water in the body can be lost without danger,

and the results of direct experiments on animals (Nothwang) confirm this supposition. Consequently it is evident that the extraordinary loss of water in cholera, especially since it is brought about so suddenly, may induce the severest symptoms and even death itself.

For our conception it is very important to remember that these symptoms which we attribute to loss of water are not peculiar to Asiatic cholera alone, but are seen in all conditions where any such loss of water is forthcoming, as in severe cases of cholera nostras. Nor is a loss of water essential; they are seen also in conditions where there is a marked deficiency of water due to obstruction to the absorption of water, as in high grades of pyloric stenosis, in which for a long time the absorption of water is limited to the smallest amounts. Such cases occasionally come into the hospital in a condition most closely resembling the stage of asphyxia in cholera: the same shrinkage of the integuments is present, the eyes are sunken, the cheeks are hollow, frequently the vox cholerica is present, and not seldom muscular cramps in the calves and other parts of the body are felt. Even the thickening of the blood is evident in the higher percentage of hemoglobin than would be expected from the wasted condition. One patient with cicatricial contraction of the pylorus, who was repeatedly admitted to hospital, generally showed on admission a hemoglobin percentage considerably above the normal for a healthy man. In order to produce an absorption of water under such circumstances it is usually necessary to introduce it per rectum, or after repeated washings of the overdistended stomach. With this treatment the patient just mentioned increased in weight 13 pounds within seven days, the percentage of hemoglobin lessened, and the previously scanty and albuminous urine increased to over 2 liters in the twenty-four hours and continued free from albumin. Another case from the hospital in this place (Tübingen) was described by Leichtenstern (1878). This was also a case of cicatricial stenosis of the pylorus, the patient presenting on admission the typical symptoms of the asphyxial stage. Besides other symptoms due to the extreme lack of water in the body, there was a pericardial friction-sound, which was referred at the hospital not to a pericarditis, but to the drying-up of the pericardium. The patient died, and the postmortem examination confirmed the clinical presumptive diagnosis.

The inspissation of the blood has a further result in clogging it in the vessels, thereby producing a general lowering of the circulation, which is in turn responsible for the cyanosis, the low temperature of the peripheral parts of the body, the defective nourishment of the tissues, and the decrease in the secretions. But this inspissation of the blood is not the only cause of the insufficient circulation, since circulatory disturbances are also seen in cases where the exudation into the intestine is by no means sufficient to produce such a thickening of the blood. A further cause of the disturbance of the circulation is to be sought in the incompetency of the heart.

The heart weakness is in part due, in cases of marked thickening of the blood, to insufficient nourishment of the heart-muscle, but partly also to the severe and extensive disease of the intestinal mucous mem-

brane, which acts in the same way as an extensive burn of the skin, or as the shock occasioned by severe wounds of the abdominal organs. As in intestinal strangulation or other lesion of the peritoneum, in perforation, in acute peritonitis, in poisoning by corrosives, a reflex heart weakness or paralysis, which may present symptoms of severe collapse, may be produced through the medium of the nerves, so in cholera the wide-spread and serious lesions of the intestinal mucous membrane may be responsible for the same.

This disturbance of circulation associated with a want of water in the tissues interferes with metabolism, added to which the metabolic end-products are only partly excreted. This gives rise to the condition which Buhl described as a sort of apparent death of the tissues, and which leads, even in the most favorable cases, to an actual necrosis or necrobiosis of many histologic elements. In many instances the heart weakness may be increased by the action on it of poisonous products from the metabolic activity of the bacilli.

This bacillary toxin has recently attracted considerable attention, and many physicians are inclined to attribute all the symptoms of cholera to its effects. In other infectious diseases also the recent trend has been to make the toxin of the specific micro-organism exclusively responsible for the essential symptoms. And it is not to be denied that it is decidedly convenient to assume such a toxin action in the case of all phenomena the explanation of which presents any difficulty. Even about the action of ordinary poisons we know but very little. True, we can recognize the symptoms and anatomic changes produced, but the mechanism or chemistry of their action, if we except corrosive poisons, and perhaps also carbon dioxid gas, is entirely unknown. We are therefore obliged and accustomed to abandon further explanation and to offer the proof of a toxic action as a sufficient explanation to account for all possible functional disturbances and also the varying pathologic changes in the cellular elements of an organ. Consequently we must not be surprised to see this ready explanation, which checks further argument, receive the widest possible extension.

That in cholera bacilli and their derivatives substances are present which act as a poison to man and animals is beyond question. Years ago it was observed (Magendie, 1832) in certain cases that the blood of cholera patients was capable of exercising a toxic effect. And more recently numerous investigators have proved a toxic action from the use of sterilized cultures of the bacilli. In fact, this powerfully toxic substance has been successfully isolated from the cultures. But, according to my opinion, we have often gone too far in the application of

these facts, and have arrived at too easy a conclusion in explaining all or almost all disturbances outside the intestinal tract as simply due to toxic action, undervaluing the significance at the same time of the loss of water, and the heart weakness due to nervous influence.

In the first place, it must not be forgotten that at the height of the attack, during the process of extreme exudation into the intestine, absorption from the bowel does not take place, or it is at least extremely limited. We see, for instance, large doses of opium exhibited at such a time producing little or no narcotic effect, and likewise, other drugs with striking physiologic effects at other times, such as belladonna, administered with no result. Only after the exudation has ceased and absorption has again set in do we find these drugs effective. Consequently it is not to be expected that at the beginning and height of the attack the toxic products of the bacilli would be absorbed and prove effective. And if it is assumed that the bacilli deep down on the mucous membrane have the opportunity of imparting their metabolic products more directly to the blood, it is at the same time to be remembered that it is precisely in the very acute cases that death results before the bacilli have penetrated deeply into the tissue of the mucous membrane in any large numbers. Therefore the severe symptoms must be explained in another way, and this is best accomplished by the consideration of the loss of water on the one hand, and the heart failure on the other. Later on, however, if the exudation has ceased, and absorption has begun, then the toxin may come into effect to explain the symptoms following an attack, especially that serious condition known as cholera typhoid, for which it is probably in a great measure responsible.

Moreover, the presumption appears likely that such toxic action takes place very early, and that the intense intestinal catarrh, the necrosis, and desquamation of the epithelium may be with justice attributed to the toxin. If we seek an explanation as to the local effects of pathogenic bacteria in infectious diseases, we may consider, on the one hand, their mechanical effects from mere contact or pressure in growth and movement; on the other, their chemical effects from the deleterious action of their metabolic products on neighboring tissues. How far the local disease may be attributed to either of these can be defined no more for cholera than for other infectious diseases; the solving of the question must therefore be left to future investigators. Yet the conjecture is legitimate that the toxin manufactured by the cholera microbe undoubtedly plays an essential part in causing the local effects.

As to the nature of the cholera toxin we are still in the dark. Yet

we can *à priori* deny the shallow hypothesis of Emmerich and Tsuboi (1893), who affirmed that because the bacillus produced nitrites, cholera was nothing more than a nitrite poisoning.

The bacilli probably manufacture many different poisonous substances, some of which may possibly belong to the ptomains, others to the toxalbumins or toxopeptones. These substances are in part excreted by the bacilli; in part they are retained in their substance, to be set free first after their death. Later on in the disease, however, various other micro-organisms may appear in the intestine and set free yet other toxins.

After this general presentation of the pathogenesis of the symptoms we will take up the more important ones, in order to study them more carefully, and indicate at the same time their prognostic significance.

[Professor Liebermeister certainly goes too far in attributing the grave symptoms of cholera to the inordinate drain of fluid from the body in the rice-water discharges and in the profuse vomiting. All analogy would point to a toxemia as the proper cause of those symptoms, and there is little doubt that the cholera bacilli in their life-period within the system develop a toxin, or toxins, which are rapidly absorbed, and in consequence produce symptoms connected with the nervous system and the gastro-intestinal tract. As Rumpf well puts it, " Cholera is essentially a poisoning of the system with the toxins of the comma bacilli."]

THE EVACUATIONS.

In a severe attack the feces lose their yellow color, and are then designated as "rice-water stools," or are sometimes compared in appearance to thin gruel. This disappearance of the yellow color is commonly attributed to the large amount of exudation and the consequent great dilution of the bile in the bowel. But a normal bile excretion would be easily sufficient to color even larger quantities of fluid; we must therefore assume that in severe cases the secretion of bile, if not checked entirely, is at least decidedly lessened.

The rice-water stools lack the peculiar fecal odor, but present instead a faint stale smell, which has been likened to that of semen. The reaction is usually alkaline, though occasionally neutral. The mucous flocculi which cloud the fluid consist of isolated leucocytes and fat drops, in addition to intestinal epithelial cells; some in small layers, and in the form of the shed covering of a single intestinal villus or as the entire lining of a tubular gland; others broken down into detritus

or converted into an amorphous slimy mass. Finally, cholera bacilli are present sometimes in small, but again in such large, numbers as to be almost in pure culture. Not rarely red blood-corpuscles are present, and when very numerous the fluid has the appearance of water in which raw meat has been steeped. As for the rest, the intestinal exudation is differentiated from the other normal or pathologic fluids of the body by its small percentage of solid matter, this amounting to only 1 to 2 %; everything else is water. Salts, and particularly sodium chlorid, are present in large amounts, while there is but a trace of albumin.

The excessive evacuations begin most frequently during the night. The fluid gushes out in a stream without force or pain. This often leads patients to imagine that with so little disturbance they cannot be seriously ill. Sometimes even in the beginning an uncomfortable feeling or slight pain is felt in the abdomen; sometimes nausea and vomiting commence early. There is frequently rumbling in the bowels, though but little gas escapes with the fluid. The evacuations follow one another in quick succession, and not infrequently several liters of fluid are passed in a short time.

With the passage into the stage of reaction the stools become less frequent and less profuse; it frequently happens that several days pass without an evacuation. In other cases a mild diarrhea still continues during convalescence, the stools becoming gradually normal in color and richer in albumin and leucocytes. Even after decided improvement a severe relapse may occur. It is likewise true that the transition into the asphyxial stage brings about a lessened number of stools, and sometimes a complete cessation of bowel action, due either to the fact that the blood permits no more withdrawal of its fluid, or that the exudation cannot be evacuated on account of paralysis of the intestine.

Vomiting sets in sometimes simultaneously with the profuse evacuations or even still earlier, but usually one hour or several hours later. It commences without effort, and the fluid gushes from the mouth in a stream. The patient feels at first relieved, but after frequent repetitions the region of the stomach becomes painful, and he himself becomes woefully prostrated. The vomited matter consists partly of remains of food, especially that taken just previously; later it resembles the rice-water fluid evacuated from the intestine. The specific bacilli are only seldom found in it. When a long enduring anuria exists, urea or its decomposition product, ammonium carbonate, may be present.

During the attack the abdomen is flat, seldom exhibits meteorism,

feels doughy, and is but slightly sensitive to pressure.   On deep palpation the splash of the fluid may be felt.   In the relaxed intestines this fluid sinks to the lowest parts; percussion therefore gives dulness, with an irregular margin, over the most dependent areas.   The epigastrium is flat or afterward may be arched on account of distention of the stomach.

The lack of bile stain in the feces is always of unfavorable prognostic import, inasmuch as the attack is then characterized as severe.   In general the danger grows with the amount of the evacuated exudation. Yet in this regard there are many individual circumstances to be taken into consideration, in that one person can stand so much more than another; children and old people or those enfeebled from any other cause may sink under moderate diarrhea.   Besides, the amount evacuated is of less importance than the amount of exudation poured into the intestine.   In fact, the worst cases are those in which, on account of paralysis of the intestine, the fluid is no longer spontaneously evacuated, but remains in the intestine and flows out only after pressure on the abdomen.   Of great importance, too, is the rapidity or slowness with which the exudation is poured out.   The sudden appearance of very profuse evacuations without previous prodromal diarrhea is rightly regarded as unfavorable; for within a few hours after this the patient may pass into the stage of asphyxia and rapidly succumb.   Yet a long-continued wasting diarrhea preceding the attack and wearing out the patient may lessen his resisting power.   Much blood in the evacuations is also unfavorable, since it points to ulcerous processes in the intestine.   Very early appearance of vomiting makes the prognosis worse.   The same is true of uncontrollable vomiting, vomiting after every drink, and persistent hiccup.

It is common to hear of a cholera sicca.   If by this are understood cases in which the exudation is not evacuated, but remains in the intestine, the term is probably hardly applicable; but such cases are seen, and especially in feeble persons death may occur before evacuation of the exudation. But if under this name cases are cited in which no pathologic exudation into the intestine has taken place, then it is likely that a wrong diagnosis has been made.

CONDITION OF THE BLOOD.

The first European cholera epidemics fell in the era when hematopathology held the field, when it was believed that especially important conclusions as to the nature of disease were likely to be arrived at from the chemical examination of the blood.   At that time, too, venesection was extensively employed, and since it was frequently prac-

tised in cholera, there was no lack of material for accurate investigation. In fact, in the blood of cholera patients at the height of the attack and in the stage of asphyxia changes were found which were important, inasmuch as they were forthcoming in no other acute disease. True, the hoped-for explanation of the peculiar nature of the disease was not discovered, yet these earlier investigations are still valuable, in that they furnish us with important aid in the critical examination of the symptoms of the disease.

At the height of the attack, and especially during the asphyxial stage, a copious venesection is often difficult. The veins are indeed full, and on opening them the contained blood flows out, but the further escape of blood takes place but slowly and drop by drop, and finally even ceases. Moreover, on account of the consequent serious lowering of the circulation, but little blood flows from the capillaries, and only by stroking and pressing can more blood be forced out. The evacuated blood is thick, coagulates but slowly, and separates less serum than normal blood. The blood-clot is dark, soft, flaccid, and reddens but slightly on exposure to the air.

Since the epidemic of 1830 an increase of urea in the blood has been repeatedly proved. Later the number of white blood-corpuscles was found increased. The essential and constant change in the blood, however, consists in a decrease in its watery constituents, or, what is the same thing, in an increase in its solid constituents. Contrary to the assertions of a few more recent observers, who have found the blood of those dead of cholera not especially thick to the naked eye, it is well to bear in mind the older and more accurate blood examinations.

While the specific gravity of the blood-serum in health is about 1.028, in cholera at the acme of the attack it is considerably higher. R. Hermann, of Moscow, found (1830) the specific gravity of the serum of blood removed from a cholera patient by venesection four hours before death to be 1.036; Wittstock, of Berlin (1832), from different cholera patients, found it to be 1.0385, 1.0447, 1.041, 1.043; Thomson, of Glasgow (1832), 1.0446, 1.0443, 1.052, 1.055, 1.057 (in the first case of this series it was pure serum; in the others there was more or less red coloring-matter); O'Shaughnessy (1832) found the specific gravity of blood-serum in cholera higher than normal—as a rule, about 1.040; Andrews, of Belfast (1832), obtained the following figures: 1.038, 1.045, 1.040, 1.040; C. Schmidt, of Dorpat (1850), found the specific gravity of the serum in various cholera patients 1.0286, 1.0334, 1.0329, 1.0470, 1.0415. The percentage of solid constituents in the serum was higher in all cases, and corresponded to the increased specific gravity; the percentage of water was correspondingly lower.

The normal specific gravity of the blood at large in healthy man is about 1.055; in woman, somewhat less. In different cholera cases C.

Schmidt found the specific gravity of the defibrinated blood to be 1.0596, 1.0662, 1.0642, 1.0648, 1.0602, 1.0711; and in one case the density of the non-defibrinated blood, 1.0728.

The normal percentage of water in the blood in healthy man is, on an average, about 78%; in woman, about 80%. The analyses of C. Schmidt showed the percentage of water in the blood of a healthy man to be 78.87%; in the male cholera patients who were examined, 76.09%, 74.53%, 74.73%; and of a healthy woman to be 82.46%; in female cholera patients, 78.61%, 76.09%, 78.06%. Wittstock obtained from the blood of a cholera patient 26.5% dried constituents; therefore there was present 73.5% of water. Andrews determined the percentage of water in the blood of 4 severe cases at the height of the disease to be 78.43%, 73.11%, 74.93%, 76.07%. Thomson found the water-percentage in his cases still further diminished; while he estimated the percentage of healthy blood at 78.39, he found in 2 cholera cases 66.121% and 67.94%.

Biernacki (1895) has still more recently given us the blood-corpuscle counts in cholera cases. This observer found, as was often found before, the number of leucocytes considerably increased; and even the number of red blood-corpuscles showed a decided rise during the attack. In the algid stage there were from 6 to 7½ millions to the cubic millimeter, and in one case more than 8 millions, a finding that is to be referred not to an increased formation in red blood-corpuscles, but to the condensation of the blood.

As in the blood, so in the tissues of the body, the percentage of water is considerably diminished. Even to the naked eye is evident the marked dryness of the subcutaneous tissue, of the muscles, and of the serous and mucous membranes. The accurate investigations of Buhl (1855) proved the percentage of water in the tissues of the body, the brain-substance, the nerves, the muscles, and the spleen to be decreased.

THE BODY-TEMPERATURE.

While other acute infectious diseases run their course with a usually typical fever, this is not the case in cholera. On the contrary, the commonly lower temperature of the surface of the body was so striking that many considered an abnormally low temperature as a characteristic symptom of this disease. The asphyxial stage was frequently designated the algid stage. As a matter of fact, the temperature of the peripheral parts of the body is indeed decidedly lowered. The thermometer in the closed fist shows frequently only 30° C. or under, and the ears and tip of the nose are often much colder. Yet the trunk of the patient is not so cold, and the internal temperature, even in presence of a lower temperature of the peripheral parts, is frequently normal or even above it.

To determine accurately the internal temperature, observations taken in the axilla are insufficient, for even if the armpit is kept closed for a long time, it does not always reach the internal temperature, on

account of the depressed circulation of the blood. For similar reasons temperature observations in the mouth are not reliable. Accurate conclusions as to the internal temperature can be drawn only when the bulb of the thermometer is inserted far into the rectum.

Even in health much more heat is dissipated from the extremities, especially the peripheral parts, than is generated in them. They retain their normal temperature only by the constant flow of arterial blood through them, which brings heat from the interior of the body. Therefore if the circulation is depressed, they become cooler and approach more closely the temperature of the surrounding air. In fact, if the circulation in an extremity ceases entirely, the temperature may fall below that of the surrounding air, on account of the continued evaporation of water from the surface. And so it happens in the asphyxial stage, if the circulation is markedly depressed, that the peripheral parts come to feel so cold to the observer's hand that the coldness is aptly described as death-like, or frequently as marble-cold, or, again, hyperbolically as icy-cold. The thermometer, too, shows an abnormally low temperature in these parts.

It is otherwise with the interior of the body. There heat is continuously produced, and its dissipation takes place only through the medium of the arterial blood in the act of conveying heat to the surface. Consequently the feebler the circulation, the greater the accumulation of heat in the interior; and it is to be expected that since heat production remains the same, every decrease in the general circulation must cause a rise of temperature within. Therefore if in the asphyxial stage, as frequently happens, with a coldness at the periphery, the temperature of the interior rises, this is not necessarily to be looked upon as fever, since it may possibly be simply the result of a defective equilibrium of the temperature as a consequence of the slowed circulation. And if, as is seen less frequently, the temperature of the interior is found normal or lower in this stage, it is a positive proof that the heat production in the whole body is decidedly below normal.

Careful simultaneous determinations of the temperature of the rectum and the axilla were carried out by Vogl. He proved that even if the thermometer was left in the axilla for fifteen minutes, its temperature was much more below that of the rectum in the algid stage than under normal conditions. The difference, which normally is about 0.5° C., and in careful estimations even less, may in cholera amount to 2° C.

The behavior of the internal temperature is different in different cases. Ordinarily with the appearance of intense exudation the temperature not only of the periphery, but also of the interior, sinks below normal. With the setting-in of the algid stage, while the temperature of the periphery remains low, that of the interior rises above normal, and may reach 39° or 40° C. During the period of reaction the ratio between the internal and external temperatures gradually returns to normal. There is, however, during this period often a rise in the temperature that may be looked on as true fever, either simple reaction-fever or a fever dependent on complications or sequelæ. And,

again, especially in severe typhoid conditions, the internal temperature may be found sinking till, at several degrees below normal, death takes place.   In the algid stage of fatal cases the internal temperature rises considerably immediately before death.   A postmortem rise also is sometimes observed.

The difference between the external and internal temperatures affords a scale for gaging the condition of the circulation, and, in general, the prognosis is more unfavorable the greater this difference is. In the stage of reaction a moderate fever of not too long duration, and not dependent on special complications or sequelæ, does not interfere with a good prognosis.   In the algid stage a lowering of the internal temperature is a very unfavorable symptom, and the same is true as regards a sinking of the temperature below normal in the period of reaction, especially if a more or less comatose condition accompanies it.

THE URINE.   CHOLERA NEPHRITIS.

With the profuse escape of fluid into the intestine the urine diminishes in quantity, becomes concentrated, but shows at first no further peculiarities.   In severe cases the secretion ceases entirely, so that none is found even on catherization.   Particularly in the stage of asphyxia is anuria common.

In a favorable case, after a few days, a scanty, dark, turbid urine appears, of moderately high specific gravity, of strongly acid reaction, and usually containing albumin.   When the percentage of albumin is high, the sediment frequently contains, besides shreds of still cohering bladder epithelium, constituents corresponding to an acute nephritis— namely, casts, usually hyaline, though sometimes granular, kidney epithelium or its debris, leucocytes, and sometimes red blood-corpuscles.   The amount of urea excreted in the twenty-four hours is at first small, and the urine is very poor in sodium chlorid.   The presence of considerable indican is of decided significance as a sign of renewed absorption from the intestine.   Ethereal sulphuric acid is increased and often aceto-acetic acid is present.   In non-fatal cases the quantity of urine gradually increases, and during convalescence may even exceed the normal, provided absorption in the bowel has again become copious.   Urea rapidly increases in amount, and on individual days in a large quantity of urine may reach twice or three times the normal twenty-four hour average.   This increase of urea is undoubtedly the result in part of the retention during the attack, and in part of the increased destruction of the severely injured tissues.   The excretion

of sodium chlorid and the other salts likewise becomes more profuse. Still later, with a favorable course, the albumin gradually decreases and the abnormal kidney constituents disappear. Yet in isolated cases this cholera nephritis may persist and prove a dangerous complication.

As to the pathogenesis of the anuria and the cholera nephritis, opinions are as yet divided. It used to be generally considered (Griesinger, Bartels, Cohnheim, Rosenstein, and others) that the kidney affection was the result of the loss of water and the severe circulatory disturbances in that organ; it was judged similar to the disturbances caused by temporary closure of the renal artery (Litten), and this view was lately taken by Leyden. Yet recently the majority of investigators are inclined to attribute it more or less exclusively to the effect of the toxin elaborated by the bacillus, making it therefore a toxic nephritis. The foundation for this view is that poisons of various kinds produce a degeneration of the kidney epithelium.

To decide the question as to the pathogenesis of cholera nephritis, it is important to take into consideration the origin of anuria. A considerable diminution of the urinary secretion is easily explained by the profuse loss of water, since it happens under other circumstances due to this cause, as in excessive sweating. Whether an absolute anuria can be produced by loss of water alone is perhaps doubtful. Yet in severe cholera cases this loss is more marked and sudden than is ever seen in other conditions, and if we add to this the serious lowering of the circulation which occurs, it may act as a sufficient explanation. Moreover, it is impossible to make the anuria an effect of the action of the toxin on the kidneys, because, on the one hand, it takes place exactly at the time when absorption from the intestine has ceased and before an entrance of the toxin into the blood can have taken place. On the other hand, we see that an inflammation or degeneration of the kidney, be it either toxic or of other origin, although a frequent cause of a decrease in the quantity of urine, yet never, as long as the general circulation keeps up at all, brings about complete suppression. If, then, we are forced to explain the anuria by the loss of water and the circulatory disturbance, there is nothing to prevent us making the same the cause of the degeneration of the kidneys. The first step in this degeneration is already noticed in the very early part of the attack, when no absorption is taking place from the intestine; and a disturbance of the function of the kidney, so marked that for a long time the urinary secretion is entirely suppressed, can scarcely pass by without leaving behind severe injury of the kidney tissue. We must consider, therefore, the cholera nephritis to be a result of the intense

circulatory disturbance brought about, on the one hand, by the loss of water and the condensation of the blood; on the other, by heart weakness. Naturally the possibility is not excluded that later, when absorption is taking place again from the intestine, the toxin may increase the degeneration.

The condition of the urine is of great importance in the prognosis. Absolute anuria is always an unfavorable symptom, because, on the one hand, by it the most serious lowering of the circulation is indicated, and accompanying it, on the other hand, are its own serious dangers. If for more than two or three days, not only is no urine voided, but none is secreted into the bladder, then the danger becomes extreme that death may result from paralysis of the heart or from uremia, due to the increase of urea in the blood and its accumulation in the tissues. In these cases urea may be excreted with the exudation into the intestine, and in exceptional cases small crystals of urea have been found on the skin (Schottin, Drasche). It is also an unfavorable sign if the quantity of urine remains long under normal, or if, after it has been for a time profuse, it sinks again. The same is true if the percentage of albumin remains large and does not soon diminish. It is favorable if there is always at least a small amount of urine excreted, and if at the end of the attack the quantity quickly increases and the albumin gradually diminishes. The continuance of a little albuminuria, even late in convalescence, provided the quantity of urine is large, has no bad significance: it may be expected to eventually cease. At least the transition of an acute cholera nephritis into a form of chronic Bright's disease, though it sometimes takes place, is very rare.

The importance of anuria in the prognosis is clearly shown in the group of statistics collected by Rumpf and Fränkel. Among about 3000 answers that they received, it was remarked in 698 cases that no anuria existed even in the first days, though there was frequently a considerable diminution of the urinary excretion; of these, 33, or 4.7%, died. In 1031 cases anuria was observed, and of these, 590, or 57.2%, died.

ERUPTIONS.

It has sometimes been believed that for cholera a specific eruption should be assumed, which, exactly like that of smallpox, measles, scarlet fever, typhus, and typhoid, was a pathognomonic sign of the disease. Moreover, this assumption was not seldom thrown out to support the theory that cholera, like these other affections, was a general disease. There is no such specific cholera eruption. And while

there are in cholera many different changes to be seen in the skin, they belong not to the nature of the disease, but to the non-specific conditions accompanying it.

At the height of the disease no eruptions are found. They appear first in the stage of reaction and in only a minority of the patients. At this time they frequently show themselves as bluish-red spots on the skin. These are to be looked on simply as places where the circulation is not yet sufficiently restored. After these are most commonly noticed small red spots, such as we designate roseola, or larger ones, such as we call erythema. These latter may appear in different forms, as erythema annulare, iridis, figuratum, multiforme. Occasionally little nodules are at the same time present, making a roseola papulosa; or peculiar blotches form, presenting the picture of urticaria; or a wide-spread reddening and swelling of the skin may look like erysipelas. Again, small hemorrhages occur, making petechiæ, or larger ones, vibices and ecchymoses. Less frequent are vesicular eruptions corresponding to miliaria, or pustules, when we may speak of impetigo or ecthyma. All these eruptions present themselves most frequently on the extremities, but may also appear in other parts of the body. True herpes labialis or facialis is very infrequent. But, besides these, we see furuncles, and a tendency to furunculosis may extend far into convalescence. Rarely there occur extensive phlegmonous inflammations, or bedsores, or gangrenous processes on the peripheral parts, as on the ears, nose, fingers, and toes.

These skin changes—especially the erythemata, the furuncles, and the gangrenous process—are in part attributable to the previous disturbed circulation, or at least are favored by it. For the others, however, particularly the urticaria, a toxin or generally foreign substance present in the blood may be responsible. The erysipelatous and phlegmonous processes usually depend on a streptococcus invasion.

The appearance of a simple eruption has in the past been considered of favorable prognostic value, and statistics show that the mortality in such cases is proportionately low. But the explanation of this phenomenon is scarcely that by the eruption some injurious substances have been eliminated from the blood, as used to be held, but that the patients who exhibit an eruption are already over the most dangerous period of the disease.

COMPLICATIONS AND SEQUELS.

The severe disturbances occasioned by a cholera attack, the intense disease of the mucous membrane of the intestine, the extraordinary loss of water from all the organs, the lowering of the circulation, which sometimes in parts amounts to almost stoppage of the blood current, lead us to expect that the patients who have survived a severe cholera attack will still be exposed to many different sequelæ.   Some of these sequelæ are the more or less direct result of the disturbances present during the attack; others consist of more accidental complications, having no direct connection with the disease, but usually not entirely independent of it, inasmuch as the resisting power of the organs to many injurious influences having been lessened by the disease has favored their appearance.   For most sequelæ both circumstances are responsible, and therefore a precise division of the sequelæ peculiar to the disease, and of the more accidental complications, is not possible.

Many sequelæ have already been discussed, as cholera nephritis, the eruptions, furunculosis, phlegmonous and gangrenous processes of the skin, and at the same time it has been shown that some of them are to be regarded as the direct result of the cholera attack.

The same is true of the deep-seated disease of the mucous membranes.   On the mucous membrane of the intestine, and most commonly in the lower part of the ileum and upper part of the large intestine, on the summit of the valvulæ conniventes, so-called croupous and diphtheritic inflammations may appear.   In rare cases, too, these may arise on other mucous membranes, in the stomach, pharynx, larynx, urinary and gall-bladders, uterus, and vagina.   These affections of the mucous membranes are not specific.   They appear in a similar way after especially severe attacks of other diseases, as typhoid fever, variola, puerperal fever.   They are to be looked on as ulcers and superficial necroses occurring in consequence of the severe disturbance of nutrition and of the circulation.   They are not caused by the specific diphtheria bacilli, but other pathogenic micro-organisms may often be in part responsible, so that it is possible in a certain sense to speak of a mixed infection.   In case of such a diphtheritis in the large intestine the evacuations are frequently tinged with blood, and there are abdominal tenderness and tenesmus, referred to the lower end of the colon.   There may be considerable fever.   During the periods of reaction and convalescence an intestinal catarrh sometimes causes a long enduring diarrhea, accompanied by meteorism, loss of appetite, and coated tongue.

As in the skin, so in many internal organs smaller or larger hemorrhages may occur. In women they are often seen in the region of the genital organs, and especially frequently in the uterus. In the last case the blood usually escapes externally, and is sometimes associated with violent uterine colic.

As a more accidental sequela is to be considered pneumonia, hypostatic as well as lobular and lobar; the last fibrinous, and with a tendency to suppuration. In the same category are hemorrhagic and simple infarcts of the lungs, spleen, kidneys, and other organs. Rare cases show a pleuritis, peritonitis, meningitis, or even, after streptococcus invasion, suppuration and abscess formation in the connective tissues, lymph glands, muscles, parotids, lungs, spleen, liver, and kidneys. Still further accidental sequelæ are bronchial or vesical catarrh, icterus, and venous thrombosis.

Entirely accidental complications are also seen. A cholera patient may be suffering at the same time from typhoid fever, a specific diphtheria of the pharynx, heart disease, kidney disease, or he may be in the throes of tuberculosis or syphilis. Such complications naturally make the prognosis much more unfavorable.

Though most patients when they recover regain their previous health, there are isolated cases showing an enfeebled constitution characterized by anemia, loss of weight, and general weakness. Not seldom an impairment of the gastric and intestinal functions remains, with a poor digestion that cannot stand certain foods, as well a tendency to diarrhea, or constipation that sometimes, especially after slight indiscretions in diet, develops into diarrhea. These disturbances usually all disappear with care in the course of time. Only rarely do we see progressive marasmus.

In isolated cases there may remain for a short time a certain amount of mental feebleness. Even mental disease has been observed as a sequela. It is usually melancholia. In habitual drunkards the attack may lead to an outbreak of delirium tremens.

CHOLERA TYPHOID.

The most frequent and important sequela is cholera typhoid. Griesinger, after comparison of many reports, reckoned that about one-fourth of all true cholera cases fell into typhoid. It appears most frequently in the second half of the first week, and occurs especially after severe attacks; in fact, in almost all patients who have passed through a moderately outspoken asphyxial stage. Many patients

who have survived the actual attack succumb to the subsequent typhoid.

The name cholera typhoid is employed in all cases where a "typhoid state" (*status typhosus*) exists. This consists in a general weakness and prostration, with a special impairment of the psychic functions. Many patients are apathetic, without interest, drowsy; they speak stammeringly, and complain of headache. Sometimes vomiting occurs, or, again, hiccup. In others consciousness is even more seriously disturbed; there is delirium, usually quiet, the so-called low muttering delirium, though occasionally active. Or there is a lethargic condition, and this may progress to actual coma, in which the patient lies unconscious, with half-closed eyes, inflamed conjunctivæ covered with mucus, and a lessened pupillary reaction. In isolated cases cramps appear in different muscle groups, in rarer cases general convulsions with subsequent coma present themselves. The tongue and lips are dry and fissured, and are often covered with a blackish-so-called fuliginous (sooty) coating. Crepitant râles are often heard over the lungs. Many cases show fever with considerable elevation of temperature, frequent, dicrotic pulse, hastened breathing, and flushed countenance. In others the body-temperature during the entire duration of the condition, or at least toward the end, is normal or even below normal, and the pulse not so rapid. Usually the urine is scanty, albuminous, and often contains abnormal constituents. The spleen is but seldom enlarged.

Many explanations have been offered for cholera typhoid. In times past it was most frequently regarded as a uremic condition resulting from disturbance of the kidney function. Or special local diseases were assumed as its cause, and, among others, morbid changes even in the brain and its membranes. More recently the condition has been looked on as the result of poisoning by the toxins elaborated by the cholera bacillus, and possibly also by other associated microorganisms. In my opinion all these theories are to a certain extent correct, but each one applies to only a limited number of cases. The endeavor to find a single explanation for all cases has been fruitless. Cholera typhoid has no unique [or simple] pathogenesis. On the contrary, under this name are included different conditions that are similar only in their symptomatology. It must be the physician's endeavor to determine in each individual case the special causes producing it. Yet I am not in favor, for this reason, of dropping the expression cholera typhoid, as has been often suggested. It is a designation to be recommended for its brevity. Moreover, it is impossible in all

cases to arrive at the exact causes of the condition, and in many, and perhaps the majority of cases, there is no single cause, but several causes cooperate at the same time to bring about the typhoid state.

In seeking for the causes that may be at the bottom of this typhoid condition, we must first of all bear in mind that the whole body of the patient, even to his brain, has been enfeebled by the attack, and especially by the disturbance of the circulation, and has therefore suffered a loss of function and of that resisting power which prevents more ready disturbance of function. It would be indeed surprising if a so-marked derangement of nutrition and metabolism in the central organs could pass without leaving any results. We can therefore in many cases attribute the cholera typhoid to the changes which the brain suffered during the attack. These changes are not of a gross anatomic nature, yet they may be sufficient to explain the disturbance of function. Such an explanation is permitted if no fever and no particular local disease exist, and if an analysis of the urine excludes kidney disease and a decided retention of urinary constituents. The prognosis in this case is comparatively favorable, in that it is to be hoped that the simple disturbance of brain function will readjust itself with time.

But in many cases there are other circumstances associated with the origin of the typhoid condition. Ailments or injuries that would produce a typhoid condition in a healthy man only by vigorous or long-continued action produce it readily in a patient with his enfeebled brain, even if they act only moderately.

Among these ailments the first to be mentioned is fever appearing during the period of reaction. This may be a simple reactionary fever or it may be dependent on a particular complication, as pneumonia, a severe phlegmonous inflammation, or other local disease. We see, moreover, that if in the very anemic or in persons enfeebled by disease fever should set in consequent on any disease, then delirium and the typhoid state are more easily brought about than in the strong and healthy. Therefore if fever is present and no other cause can be found, we may attribute the typhoid condition to it. The prognosis in such cases is essentially dependent on the nature of the fever or the seriousness of the local disease producing it.

In some cases uremia is evidently the cause. And even here one must remember that the brain is enfeebled, and consequently more susceptible to uremic intoxication. This explanation holds good in cases that show by the small quantity and the analysis of the urine severe kidney disease, violent headache with vomiting, and especially convulsions with subsequent coma. The prognosis in general is un-

favorable, yet if no other local disease is present and the urine becomes quickly normal, a favorable outcome is not impossible.

Finally, the typhoid condition may be due to the action of toxins elaborated by the cholera bacilli or other micro-organisms. Since in this stage of the disease intestinal absorption has been restored, different toxins may be taken up by the blood and produce their effects. This can be predicated of a case exhibiting no fever or marked local disease, and particularly no kidney trouble. And the possibility of its association with other causes must be considered in numerous other cases. Our discussion has therefore proved that we have good grounds for believing the typhoid condition to be a result of several causes which act more readily on account of the enfeeblement of the brain.

[There are many objections to the use of the term cholera typhoid, which has been handed down from the older authors. Rumpf ("Twentieth Century Practice") prefers to designate the condition hitherto known by this name, in order to avoid misunderstanding, as coma following cholera, or the comatose stage of cholera.]

ABORTIVE CASES.

In a cholera epidemic, besides the severe we see mild cases, which etiologically belong to cholera, since they are caused by the specific micro-organism, but which lack the serious symptoms and dangers of an outspoken case.

Cases presenting the characteristic symptoms, but in lessened degree, are termed light grade cholera, or cholerine. Without or with a prodromal diarrhea, there appears a series of watery evacuations that do not lose entirely their yellow color. Frequently, also, there is vomiting. There is a feeling of prostration, with discomfort and oppression over the stomach; the pulse is often weak, but never entirely disappears; the temperature of peripheral parts may fall somewhat; the urine is scanty, but never suppressed; in isolated cases there are muscular cramps. The previously strong may succumb to such an attack, and at any time an increase in the stools may result in a transition to outspoken cholera with its rice-water discharges. But if the evacuations soon cease and no relapse sets in, quick recovery usually follows; yet reactionary symptoms or even a mild typhoid condition may occur.

The mildest cases are designated cholera diarrhea. In these there appears only what would correspond to the prodromal diarrhea, lasting

a few days, a week, or even longer, but then ceasing without any more marked symptoms. Whether this will be all, or whether a cholera attack is going to follow, cannot in individual cases be determined. Yet the course depends, in part at least, on the behavior of the patient, especially with regard to diet.

In some epidemics the cases of cholerine and cholera diarrhea seem to be more numerous than those of frank cholera. Still, there are many cases of diarrhea due to other causes, and which are therefore not to be considered as cholera. The only method of positively differentiating these from cholerine and cholera diarrhea is by the examination of the stools for cholera bacilli.

Finally, in late years it has been frequently observed that during an epidemic certain individuals suffering from neither diarrhea nor other cholera symptom show in their stools true cholera bacilli. These are cases of infection without clinical symptoms, in which it must be assumed that either the bacilli had not their full virulence, or, what is more probable, that these individuals are insusceptible. These observations are of especial importance, since they clearly show, on the one hand, that at the time of an epidemic errors in diet or other indiscretions may result in an outbreak of cholera; and, on the other hand, that a person perfectly well himself may possibly introduce the disease from one place into another. Moreover, convalescents from cholera, sometimes may harbor even for weeks in their intestinal tract bacilli capable of evolution.

ANATOMIC CHANGES.

WHEN death results at the height of the attack or in the asphyxial stage, the postmortem shows, on the one hand, pathologic changes corresponding to an acute intense catarrh of the intestine, and especially of the small intestine; on the other, the effects of an uncommon loss of water from the blood and tissues, and of a serious disturbance of the circulation. In general, gross macroscopic changes in the organs are not seen. The more rapid the death, the slighter the visible postmortem changes. On this account the postmortem appearances in cases, previously enfeebled by other diseases, that succumb quickly to cholera are, as far as the cholera is concerned, comparatively insignificant. This is also frequently true of the first cases of an epidemic in which the attack is especially severe and rapidly fatal.

For this reason the view has often been expressed that the pathologic changes in cholera are not in proportion to the severity and malignity of the disease, and that therefore cholera, like typhus, which exhibits a like disproportion between the symptoms and the pathologic appearances, must be a general disease associated with as yet but imperfectly understood processes in the blood which destroy life by their toxic effect or in some other manner. But this assertion is, in point of fact, based on unstable ground. If the processes present in the intestine and their results are correctly estimated, the postmortem finding will be seen to fully correspond to the symptoms observed during life. In relation to this I refer the reader to the earlier discussions on the pathogenesis of the symptoms (p. 348).

In case of death during the attack or in the asphyxial stage, the entire body seems shrunken, the skin is wrinkled and shriveled, the eyes, usually half-open and exhibiting a dried-up appearance in the uncovered parts, are deep in their sockets, the nose is pointed and projects, the cheeks are hollow and the jaw-bones prominent; the fingers are bent, the arms and legs are flexed, and the muscle bellies stand out (the so-called "boxer-pose"). The cyanosis present during life is still visible in a dark more grayish color of the whole surface. Many parts of the skin still show an injection of the small veins in a bluish-gray or violet staining, especially of the lips, nails, fingers, and toes. Postmortem rigidity sets in early, is strongly marked, and lasts long. At its appearance remarkable movements of the extremities, and espe-

cially the fingers, often appear. Sometimes a postmortem rise of temperature is observed. The body cools slowly. Decomposition occurs late, probably on account of the small amount of water.

The subcutaneous tissue is markedly firm and dry. The muscles show a dark red color. The majority of the organs are characterized by an unusual dryness. The serous membranes are remarkably glossy, on account of a tenacious, slimy, stringy exudate composed of desquamated epithelium, in part undergoing mucoid change. On the mucous membranes, too, the epithelium is in places loosened or desquamated. The blood is for the most part accumulated in the great veins and in the right heart. It is dark, thick, and presents flabby, dark, or sometimes buffy clots. The colorless corpuscles are increased.

On opening the abdomen, besides the slippery and sticky slimy membrane on the surface of peritoneum, the striking peculiarity is the rose-red color of the small intestine throughout, or at least in its lower part, the result of intense injection of the vessels, while the stomach and large intestine usually retain their normal color. The coils of intestine are still full and distended. The quantity of fluid yet within the whole intestinal tract not infrequently amounts to from 3 to 4 liters. In the lower part of the ileum and in the large intestine this fluid shows an alkaline reaction, while in the stomach there is usually still an acid reaction. The fluid corresponds in its nature to our previous description of the rice-water discharges. It often contains large epithelial flakes, which have in part desquamated during life. The mucous membrane of the intestine nowhere displays any bile stain. In the small intestine, and especially in the region of the ileocecal valve, it is reddened, the finer veins are deeply injected, the mucous membrane frequently shows smaller or larger hemorrhages, and more or less blood is often mixed with the contents of the bowel. Less frequently we find that the injection of the mucous membrane has already disappeared in the dead body. The mucous membrane is in a greater or less degree edematous, and not rarely this swelling extends to the other layers of the intestinal wall, so that the whole bowel seems remarkably heavy. Otherwise the mucous membrane shows no gross lesions, and more accurate examination is required in order to detect further mischief. In some situations, and often over quite an extensive area, the epithelium is wanting, and where it is still preserved it is easily stripped off. The villi are necrosed here and there on their summits, or even throughout the greatest part of their tissue. The intestinal follicles—as well as the solitary glands and Peyer's patches —are often surrounded by an area of intense hyperemia; they are

swollen often to the size of a hempseed and over, sometimes in conse-
quence of a more solid infiltration, sometimes by the absorption of
liquid which can be increased postmortem by diffusion of the fluid
contents of the intestine. Individual follicles are often ruptured, and
the rupture of many of them in a Peyer's patch may give it a reticu-
lated appearance. The specific cholera bacilli are found not only in
the intestinal contents, but also, and very often, in small aggregations
in the intestinal wall, especially in the convoluted glands and villi, and
occasionally in the deeper layers of the mucous membrane and in the
submucous tissue. In individual cases the upper part of the large
intestine shows a similar injection and swelling. The stomach is filled
with fluid in which remnants of food are sometimes found. The gas-
tric mucous membrane exhibits no constant changes. It is sometimes
entirely or in part hyperemic, is often covered with tenacious mucus,
is sometimes swollen, and displays not infrequently small ecchymoses.
As an occasional and accidental lesion in the intestine, must be men-
tioned the recent invaginations arising during the death agony. The
vessels of the mesentery are filled with blood; the mesenteric glands,
especially those corresponding to the lower part of the small intestine,
are frequently swollen to a slight extent.

The other abdominal organs, with the exception of the kidneys,
show few characteristic lesions. The liver is bloodless, dry, soft, and
friable. The gall-bladder contains a thick dark bile, which on pressure
is readily evacuated into the duodenum. The spleen is small, soft,
wrinkled, and on section is bloodless and dry. In women hemorrhages
are frequently found on the mucous membrane of the uterus, in the
ovaries, and not seldom in the parenchyma of the genital organs, and
in the subserous tissue.

The kidneys show no striking macroscopic changes. On section
they are dark red, on account of venous hyperemia, and the cortex is
slightly swollen. But microscopic examination shows evidently be-
ginning degeneration. The epithelium of the cortex is in a condition
of cloudy swelling, with here and there destruction of the protoplasm,
or it contains even fat corpuscles. In the convoluted tubules are
often found hyaline casts and epithelial debris. In the pelvis of the
kidneys there is usually a more or less slimy fluid containing desqua-
mated epithelium. The urinary bladder is empty or contains a little
mucus or a small amount of cloudy urine.

The sinuses of the dura mater and the arteries and veins of the
brain and its membranes are filled with dark thick blood. Not seldom
small ecchymoses are found. The brain-substance shows no particu-

lar lesions. In the ventricles a little fluid is frequently seen. The pia mater is sometimes slightly edematous. The lungs retract well on opening the chest. The pleuræ show the same viscid deposit that is found on other serous membranes, and often small hemorrhages in addition. The lungs are very dry, in the dependent parts somewhat hyperemic. Otherwise there is neither edema nor hypostasis. The large and small bronchi contain no fluid, and only here and there a little tenacious mucus. The pericardium contains no, or only a few drops of, fluid, and in some cases it is as dry as parchment. Within it and on the epicardium near the base of the heart small ecchymoses are frequently found. The left heart is usually contracted, the right is dilated and filled with blood. The pulmonary arteries, and often the commencement of the aorta, contain a considerable quantity of blood. The other arteries are contracted and empty.

When death takes place at a later period, and especially after a typhoid condition, the lesions are quite different, and more so the later death occurs. The signs of the loss of water and the severe circulatory disturbance have decreased or disappeared. The external appearance of the body corresponds more closely to that observed in those dead from other diseases. The cyanosis has vanished, the shriveling of the skin is less or no longer present, the postmortem rigidity is feebly marked, decomposition sets in earlier. There is often a black coating on the lips, tongue, and gums, and not rarely thrush also is found in the mouth and pharynx. The subcutaneous fat and the muscles are no longer dry, the epithelium of the serous membranes has in great part become regenerated, and they show once more their wonted smooth, moist, shining surface. In the intestine the injection of the serous and mucous membranes has passed away. It is no longer filled with a watery exudation, but contains instead normal pappy and yellowish fecal masses; gases are again present, and sometimes also considerable quantities of mucus. The intestinal mucous membrane frequently shows an almost normal appearance, the hyperemia has disappeared, the epithelial coating is in great measure restored, the follicles are no longer swollen. In other cases are found remains of hemorrhages, or of intercurrent croupous and diphtheritic inflammations or their results in more or less deeply excavated ulcers. In these ulcers are found large numbers of different kinds of micro-organisms. In many cases cholera bacilli can no longer be obtained from the intestinal contents or the mucous membrane, yet occasionally they are seen for fourteen days after the beginning of the disease or even longer. The other abdominal organs are, again, richer in blood and are of normal

size. The spleen is in individual cases enlarged, and occasionally shows infarcts. The gall-bladder is filled with thin bile.

In the kidneys the lesions are further advanced. The organs themselves are larger; than normal the capsule is tense, but strips easily. The cortex is especially swollen, and shows on section less blood, a pronounced cloudiness, and a pale reddish or yellowish color, while the hyperemic medullary pyramids show through their dark-red color. The cortical epithelium is in great part degenerated. It contains fat granules, or is broken up into a detritus, or is in the condition of coagulation necrosis. In the convoluted tubules and loops are found hyaline and granular casts, fatty detritus, and remains of broken-up epithelium. The glomeruli usually show little change. In the third week after the commencement of the disease the epithelium of the convoluted tubules is already considerably regenerated. The bladder is again filled with urine, though this often contains albumin and casts. The vesical mucous membrane frequently shows ecchymoses, and sometimes croupous or diphtheritic exudations. In women the uterine and vaginal mucous membrane may show the same.

The cerebral pia mater usually exhibits more or less edema, and the ventricles of the brain contain more fluid than normal. In the lungs are frequently found hypostatic consolidation or edema, sometimes infarcts as well, or the different pneumonic processes mentioned under complications. The bronchi are often markedly hyperemic and contain considerable mucus. In the pericardium, again, more fluid than normal is found. The heart is flabby and frequently contains firm fibrinous clots. The right heart is usually still distended and filled with blood. The blood is thinner and not so dark as usual. Not infrequently the evident commencement of parenchymatous degeneration is to be observed in different organs, the liver, the salivary glands, muscles, and especially the heart. Other changes corresponding to the previously mentioned complications are also found, especially more or less extensive croupous exudations and diphtheritic ulcers on different mucous membranes. The eruptions present during life are usually no longer recognizable on the cadaver, with the exception of hemorrhages, furuncles, and phlegmonous and gangrenous processes.

Finally, many pathologic lesions may be found that have nothing to do with cholera, and correspond only with accidental complications.

DIAGNOSIS.

THE symptoms of cholera are so striking and characteristic that in by far the largest number of outspoken cases the diagnosis is easy, and the malady can be recognized, as a rule, by a lay person. The differential diagnosis from cholera nostras may usually be made through the greater extent of the epidemic, the decidedly severe course, and greater mortality of true cholera. Yet difficulties occasionally present themselves. Discussions have more than once arisen at the beginning of an epidemic as to whether it was true Asiatic cholera or cholera nostras. Yet these have been most frequent in cases where it was desired to conceal as long as possible the presence of true cholera. Still, the above-mentioned facility of diagnosis is true only in general and not in individual cases. The aged, consumptives, or those otherwise enfeebled may die of cholera before characteristic symptoms appear. Moreover, in the course of an epidemic it often happens that cases of cholera nostras are not differentiated from true cholera, and cases of intestinal obstruction or peritonitis with vomiting and serious collapse are regarded as cholera by persons who have heard of cholera sicca. Acute poisoning with arsenic, salts of copper, tartar emetic, or bichlorid of mercury may at the time of a cholera epidemic be mistaken for cholera. In such cases of poisoning a medical man ought not to find the differential diagnosis difficult, for, besides the history, violent vomiting usually precedes the diarrhea, the vomited masses often contain blood, the evacuations are less profuse and have no rice-water appearance, and there is intense pain. Yet where medical observation is wanting an error is easy.

In 1867, as member of the Board of Health in Basel, I took part in the diagnosis of a case that was considered to have died of cholera. For the sake of prophylaxis the patient's linen, bedding, etc., had already been burnt. The postmortem findings were such that cholera might readily have been assumed to be present. Among other evidences zooglea masses were found in the intestine, a point to which Klob had just drawn attention. But several slight erosions and superficial ulcers in the gastric mucous membrane excited suspicion, and the examination of the stomach-contents showed at once that it was a case of acute arsenical poisoning. This case was described by C. E. E. Hoffmann.

The diagnosis may be especially difficult in the first cases when no epidemic as yet exists. But these first cases frequently declare their

true nature during life by a particularly violent and rapidly fatal course, extremely profuse evacuations, quickly followed by symptoms of severe circulatory disturbance, and deficiency of water in the body, and, postmortem, by a rose-red color of the small intestine, a large amount of rice-water fluid within it, and an empty bladder. Yet an uncommonly severe case of cholera nostras may present similar symptoms. And if the question is one of imported cases, even these may run a longer course, or prove to be abortive cases, which have little that is characteristic about them; and it is exactly in such cases that the diagnosis is of especial importance, for it is only when they are early recognized that we can hope to suppress the epidemic at its outset. Moreover, it is as bad to call every suspicious case cholera, and thereby cause unnecessary uneasiness among the population, as to overlook a true case and leave the way open for an epidemic. Fortunately, we possess to-day in the examination for cholera bacilli a means of decisively recognizing almost all cases. When the result of the examination is positive, there is no doubt about the disease being cholera; when after correct and careful examination it is negative, though there is not the same certainty, it is highly probable that the presence of Asiatic cholera may be denied.

R. Koch (1893) has given us an accurate method for the examination of cholera bacilli as carried out after much experience at the Institute for Infectious Diseases. It is divided into the following parts:

1. *Microscopic Examination.*—A mucous flake is picked from the material to be examined (the evacuations of the sick or the intestinal contents postmortem), spread and fixed on a cover-glass, and stained with a dilute Ziehl's fuchsin solution. These preparations sometimes show the cholera bacilli in pure culture; in other cases mixed with the ordinary intestinal bacteria, among which the Bacillus coli predominates. In other cases, lastly, the cholera bacilli are no longer recognizable. When present in pure culture or in overpowering numbers, together with Bacterium coli, the cholera bacilli, especially in those places where the mucus is drawn out into threads, are arranged as a rule in characteristic groups, in which almost all the organisms point in the same direction. Yet even when this characteristic grouping is wanting, provided numerous bacteria with the appearance of cholera bacilli are present, and, in addition, only Bacterium coli, the diagnosis of cholera may be made with certainty. In this simple manner about half the cases can be diagnosticated in a few minutes, and so far the completion of the evidence, which should never be omitted, has in all cases confirmed the preliminary or provisional diagnosis.

2. *Peptone Culture.*—One or more loops of platinum wire armed with the fluid to be examined or the mucous flocculi is introduced into a sterile solution of 1% peptone and 1% NaCl, which, if not evidently alkaline, is made so by the addition of sodium carbonate. The solution is then allowed to stand at 37° C. As soon as the fluid becomes at all cloudy a drop is taken from the surface with a loop of platinum wire and examined microscopically. If the cholera bacilli were present in large numbers in the original material, they may be found after six hours in pure culture on the surface of the peptone solution. If they were in fewer numbers originally, the cholera bacilli appear later on the surface of the peptone and more or less mixed with fecal bacteria (principally Bacterium coli), so that the examination may leave doubt as to whether we have to deal with true cholera bacilli or not. Still, if they were present at all, further examination and isolation are made easier. It may also be of advantage to cultivate at once a second generation in peptone solution from the first peptone, in which it was possible to recognize only a few comma bacilli, in order to obtain them in larger numbers. Later on the cholera bacilli on the surface of the peptone are overgrown and forced out of existence by other bacteria.

3. *Gelatin Plate Culture.*—The colonies of cholera bacilli are so characteristic on the gelatin plate that this culture must not be omitted. Even when the direct employment of this procedure leads to no positive result, thoroughly characteristic colonies may be obtained by cultivating a second generation from peptone. The best temperature for a well-prepared 10% gelatin is 22° C. At this temperature the colonies attain their characteristic appearance in fifteen to twenty hours. A higher temperature would favor the growth of the colonies, but would at the same time liquefy the gelatin and allow the colonies to run together.

4. *Agar Plate Culture.*—The culture-material is spread over the surface of the agar plate. The colonies are less characteristic than on gelatin and require for recognition the aid of the microscope. The advantage of the procedure lies in the fact that the agar can be kept at a temperature of 37° C. and thereby produce a sufficient growth of the colonies after from eight to ten hours.

5. *The Cholera-red Reaction (Indol Reaction).*—For a long time it has been known that the intestinal contents of a cholera patient give a red color with nitroso-nitric acid. Pure cultures of cholera bacilli—as was discovered by Poehl, Bujwid, and Dunham—are also stained from rose to a deep red by the addition of pure sulphuric or hydrochloric

acid, due to the production of nitroso-indol, the so-called cholera-red. This color appears on the addition of an acid only when indol and nitrous acid salt are present. Both these are elaborated by the cholera bacillus, the former from the albumins in the medium, the latter by the reduction of nitric acid salts which are present. There are many other bacteria also that produce indol, and others that reduce nitrates to nitrites, but until a short time ago there were no bacteria known that did both, and that at the same time resembled cholera bacilli so as possibly to be confused with them, and therefore R. Koch attributed to this cholera-red reaction a very high diagnostic value. And although this reaction can no longer be regarded as absolutely characteristic, since it has been found in connection with other comma bacilli (M. Neisser, C. Günther), it has yet a certain importance when associated with other criteria. The reaction is best carried out in peptone cultures.

6. *Animal Experimentation.*—A small amount of a culture grown on agar, divided in a little sterile bouillon and injected into the peritoneal cavity of a guinea-pig, kills the animal. Before its death there is a fall of temperature.

These methods, and especially the first one mentioned, are in the majority of cases sufficient for a positive recognition of cholera bacilli. Yet it is always desirable, when practicable, in a case where the diagnosis is important to leave the differential diagnosis to one thoroughly versed in bacteriologic methods. And there are instances in which even the most expert observers fail to come to a positive conclusion, even with all these methods. In recent years so large a number of micro-organisms with the greatest resemblance to cholera microbes have been discovered that the diagnosis of cholera bacilli has become somewhat uncertain. In relation to water microbes especially the question whether or not they are actual but degenerated descendants of true cholera organisms has not yet been definitely settled. True, this uncertainty is of theoretic rather than of practical importance, since it does not really arise in the examination of the evacuations or the intestinal contents. Yet the discovery of a further differential criterion is to be earnestly desired. Perhaps R. Pfeiffer's reaction will prove such a criterion—namely, that the blood-serum of animals immunized to cholera exercises a specific fatal effect on cholera bacilli while other bacteria are unaffected. The corroborating investigations of Dunbar (1895) add the hope that this method may also be applicable for the differential diagnosis of other pathogenic bacteria morphologically similar to one another.

The discrimination of outspoken and very mild cases of cholera is practically of secondary importance. Ordinarily cases of cholerine and cholera diarrhea are not reckoned in cholera statistics, although etiologically they belong to cholera, and this is without doubt justifiable as far as mortality statistics are concerned, since they are practically never fatal. The boundary between cholerine and frank cholera is more or less arbitrary, in that all stages between the two are met with. All cases are commonly considered frank cholera in which the evacuations fail to show bile stain, or that show complete anuria or an asphyxial stage or are followed by a severe cholera typhoid.

PROGNOSIS.

CHOLERA is one of the most dangerous diseases. Of all diseases appearing in great epidemics, it has, next to plague, the highest mortality. Still, the mortality in individual epidemics is not always the same. Moreover, the statistics of different observers cannot always be compared, because the boundary-line is never drawn in exactly the same place between frank cases, which are usually the only ones reckoned in statistics, and mild cases, which, as a rule, have no mortality. Nevertheless it can be generally estimated that about half the patients with outspoken cholera die. In extensive and long-lasting epidemics as they occur in large cities, the mortality is commonly under 50%; in smaller epidemics, especially in towns, it frequently exceeds 50%. As a rule, the mortality is highest at the beginning of the epidemic, so that frequently during its rise more than half of those attacked die. It is during this period especially that the very rapid so-called foudroyant cases, with death in a few hours, make their appearance. Toward the close of an epidemic the mortality descends below, and sometimes considerably below, 50%.

Death occurs most frequently during the actual attack in the course of the first or second day, although there are many who pass successfully through this stage who afterward succumb in numbers to the complications. All important complications and sequelæ, especially the appearance of a marked typhoid condition, are unfavorable from a prognostic point of view.

According to the statistics of Rumpf and Fränkel compiled from the hospital cases of the Hamburg epidemic in 1892, there were, altogether, 7870 patients treated, of whom 3806 died. Of these latter, 1741 died within twenty-four hours after the beginning of the attack, and 663 in the course of the second day. In other words, almost two-thirds of the deaths took place in the first two days.

Of the 474 cases that lived through these two days, but in whom secondary symptoms made their appearance, 230, or almost one-half, died; while of 238 in whom no secondary symptoms were noticed, only 30 died. Among the secondary processes, by far the most favorable from a prognostic point of view is simple fever without complications. Among 170 cases of this kind that exhibited in part a single rise of temperature, in part a remittent fever, seldomer a continuous fever for several days, there was no death. Less favorable are cases followed by ulcerative intestinal processes, pneumonia, or delirium. Fever associated with or followed by coma is likewise unfavorable; of 41 such cases 25 died. By far the most unfavorable condition was coma without preceding fever, especially when accompanied by a subnormal temperature, when there was only a slight rise shortly before death; of 183 of these cases, 165 died.

The degree of danger in individual cases depends in a great measure on the resistance of the patient, and therefore many particular circumstances must be taken into consideration.

Age is of great importance. Children under ten show a high mortality, and it becomes higher the younger they are. The same is true for the opposite end of life. After fifty the prognosis is very unfavorable, and patients aged seventy or upward but seldom survive the disease. Middle life gives a better prognosis, and this is explained, in addition to other circumstances, by the proportionately low mortality among soldiers in barracks during peace.

Sex is of less importance, though in women the average mortality is possibly somewhat less. Pregnancy greatly increases the danger. In severe cases the fetus usually dies, and, if the woman does not succumb, she aborts or miscarries during the period of reaction. Subsequently diphtheritic processes may appear in the uterus and vagina. It is a remarkable fact that in suckling women, while all other secretions are suppressed, lactation frequently continues.

Of more importance are the previous health and earlier habits of life. Preceding acute or chronic disease, irregular life, want, or privation not only increase the susceptibility, but also make the prognosis worse. Habitual drinkers give a very bad prognosis. Finally, the manner of treatment and nursing is of importance. Under unfavorable external conditions the mortality increases, as among the pilgrims huddled together in great numbers at Mecca; at pilgrimage places in India; on emigrant, pilgrimage, and coolie ships; in armies while in the field; and, finally, at home in many country and city places where there are too few hospitals. Moreover also, the carrying of a patient too far to a hospital has an unfavorable influence.

In individual cases the danger depends essentially on the severity of the disease. A previously healthy man rarely succumbs to cholerine or cholera diarrhea, but with the intensity of the symptoms his danger increases. The prognostic importance of individual symptoms has already been discussed, particularly that of the evacuations, vomiting, temperature, urinary excretion, the eruptions and complications, and especially the condition known as cholera typhoid. Even in a marked asphyxial stage recovery may be reckoned on in about one-fifth of the cases. Still, as regards prognosis, it must never be forgotten that cases which set in at first in a mild form may suddenly become severe and end fatally with symptoms of asphyxia, and that, on the other hand, patients with the most intense symptoms may notwithstanding recover contrary to all expectation.

TREATMENT.

A VERY wide-spread popular opinion, which is likewise shared in by many physicians, considers cholera to be a disease in which treatment is of little avail. This view is correct in relation to the treatment that begins first when the patient is already at death's door from the attack. But it is incorrect as applied to the treatment that is begun earlier and that seeks to prevent the serious danger to life of the attack. Striking results have been obtained in the treatment of the so-called prodromal diarrhea, which is actually part of the disease, in fact, a stage in it in which it is still susceptible of cure. But results of measures for the prevention of the disease have been even greater and more effective. It is by means of prophylaxis, as developed in our own day through our increased knowledge of the etiology, that cholera has lost the greatest part of its terror. And in the future prophylaxis will undoubtedly remain the most important feature in the treatment of this disease.

PROPHYLAXIS.

We distinguish a general and an individual prophylaxis. The former embraces all measures by which the origin or spread of the disease may be prevented; the latter gives rules by which the individual may protect himself against the disease. These prophylactic precautions have been deduced principally from the etiology, yet it is possible to assert that the theoretic precautionary measures also have been proved by experience to have been judicious.

In the theoretic consideration of prophylaxis we may employ von Pettenkofer's scheme of regarding a cholera epidemic as the product of X, Y, Z. In this, X signifies the specific cause, Y the predisposition of time and place, and Z the individual predisposition, or susceptibility. When one of these factors $= 0$, the whole product $= 0$; or, in other words, a cholera epidemic cannot arise if the specific cause of the disease is not present, if the predisposition of time and place is insufficient, or if individual susceptibility is lacking. Consequently if we can succeed in completely doing away with one of these three factors, the problem of general prophylaxis is solved. But against which of the three shall the attack be directed? Opinions on this point are more or less divided. The bacteriologic school, headed by R. Koch, insists that without neglecting the other factors the struggle should be particularly directed against X, the specific cause. Von Pettenkofer and his followers attach but little importance to this, and assert that the causes of the predisposition of locality, or Y, should first be removed. And, lastly, Ferran and the other believers

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in prophylactic inoculation would like to see the end attained by the removal of Z, the individual predisposition. It is evident that if any of the three parties were completely successful in their aim, the occurrence of an epidemic would be impossible. But, unfortunately, so far none of them, although they have accomplished some very practical results, have succeeded in annihilating the object [or factor] attacked, by which alone the risk of an epidemic would become impossible. Under these circumstances it is without doubt best to keep an eye on all these factors and endeavor to minimize each as far as possible. Then at least we shall have succeeded in making the product—namely, the probability of an epidemic arising—as small as possible. The diminishing of X and Y is principally the office of general, while that of Z falls into the province of individual, prophylaxis.

GENERAL PROPHYLAXIS.

The problem of general prophylaxis is the prevention or limitation of cholera epidemics.

When, through the remarkable discovery of R. Koch in 1883 and 1884, the specific cause of cholera became known, and was, as it were, put within our grasp, there was every ground for the hope that thenceforth we could pluck up the evil from the root, and by setting aside the exciting cause, von Pettenkofer's X, at will prevent the origin and spread of an epidemic. As is well known, this hope has been only partly fulfilled. Among others, the great Hamburg epidemic of 1892 taught us that the knowledge of the nature of the foe was not sufficient to ward it off with certainty. At Hamburg the predisposition of locality was so great, on account of the shocking condition of the water-supply, that, given an introduction, an epidemic could not be avoided. At the same time it is a matter for congratulation that the numeric extent of the epidemic remained so limited. For although the disease was carried in all directions to such an extent that, in the year 1892, 267 places in Germany reported cholera, and, in 1894, 157 places, and although the danger of an introduction from Russia remained always present, Germany suffered but little in comparison with the epidemics of previous years, and for this she has to thank the intelligent measures of the authorities and the disinterested activity of scientific physicians. In the three years of 1892–94 including the Hamburg epidemic, not many more than 10,000 people died of cholera, while in Russia during the same time about 800,000 succumbed.

The recognition of the fact that cholera cannot arise without the specific bacilli, and that these are disseminated but short distances through the air, led at once theoretically to the conclusion that isolation would prevent the spread of the disease. Opinion is divided as to the practical effect of isolation and quarantine measures. Not only

the physicians who advocate the importance of the predisposition of locality, and therefore attribute a secondary rôle to the cholera bacillus in the rise of an epidemic, declare all isolation measures to be misdirected and ineffective; but, remarkable to say, so also do many workers in bacteriology. To this opinion they can reckon on the assent of tradesmen, whose interests are severely injured by isolation, and of that part of the public in whom fear of the disease does not overcome their aversion to the annoyance attending isolation.

To be secure, the isolation must be complete, and must affect not alone those who are manifestly ill, but even the seemingly healthy and their household goods. Such complete isolation is but seldom possible. With as little success as is met with in an attempt to absolutely prevent smuggling can complete isolation usually be carried out. Yet where it was possible to thoroughly carry it out, it has had its effect. Thus, for example, in 1831 the Russian court, embracing some 10,000 persons, strictly isolated in Peterhof and Zarskojeselo, remained free from the disease. Griesinger with much labor endeavored to find an instance where cholera broke out on a small island after the lapse of a long time from the arrival of any ship, but his search was in vain. We can easily explain why the isolation frequently carried out in the first epidemics by means of lines of troops, and the later limitations of traffic, were without avail, if we reflect that these regulations were executed after the disease had already passed the boundary, and that, moreover, seemingly healthy persons were not subjected to quarantine. Strict quarantine in seaports has in numerous instances prevented the introduction of the disease. Even so recently as 1892 the United States remained free from cholera on account of the quarantine regulations applied to Hamburg ships; in reference to the rigorous carrying-out of those regulations complaint was made, perhaps with some justification. Ordinary isolation is sometimes not without effect. St. Petersburg in 1830 and 1831 was spared from cholera so long as the military cordon intrusted with the duty of enforcing quarantine was maintained; it was only after these troops were removed, partly because the danger seemed past, and partly because the insurrection in Poland gave them employment elsewhere, that cholera appeared in St. Petersburg (June, 1831). And although under ordinary circumstances von Pettenkofer's dictum may be correct, that traffic can never be considered free from danger ("pilzdicht"), it by no means follows from this that all limitations of traffic are to be rejected as useless. In innumerable cases the disease has been introduced when simple isolation and quarantine regulations could have prevented it.

In this, as in so many other things, the conflict between theory and practice can be averted only by a compromise. And if complete isolation is possible only in exceptional cases, it must still be regarded as the ideal to be approached as near as circumstances will allow. It is even of great importance if at the time of an epidemic traffic is limited, at least as far as it is possible without injuring important interests. If, for example, all concourses of men such as take place at annual fairs, popular celebrations, and in connection with pilgrimages and concentrations of troops were stopped. In seaports strict quarantine for all ships coming from cholera-infected regions is of undoubted benefit.

Similar principles of strict isolation have been repeatedly laid down by successive International Sanitary Conferences. If the result does not correspond to the expectation, it is in a great measure due to their being carried out in an incomplete manner, leaving much to be desired.

At present there are in almost all countries regulations more or less restricting traffic with countries or seaports in which cholera exists. In the "Denkschrift über die Choleraepidemic 1892" may be found accurate information as to the measures adopted by different European and the most important extra-European states for this purpose.

More important than the limitation of traffic is the careful inspection of travelers arriving from a cholera region, the isolation and strict observation of every suspicious case, and the promptest possible determination of the diagnosis by bacteriologic examination. These precautions are exceedingly difficult, and can scarcely ever be carried out in their entirety, yet even when incomplete serious evil may be avoided.

Persons traveling by railway who exhibit a typical attack are usually recognized as cholera patients by the conductors [guards] or other passengers, but the milder cases are especially dangerous, since they are not always recognized even by the most careful medical control. Lastly, many persons come over the boundary from an infected region on foot or by means of conveyances other than the railroad. Therefore it is of great importance to inspect medically all persons arriving or sojourning at hotels and lodging-houses, almshouses, and asylums. Complete control of foreigners *en passant*, who often arrive in multitudes, is especially difficult.

Since cholera is introduced with especial frequency by water traffic, boats and ships must be carefully watched. In Germany in 1892 special inspectors in addition to the statutory medical staff were

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appointed in the various river districts, whose duty it was to arrange control stations for the inspection of vessels and their passengers. Moreover, vessels were restrained, under pain of punishment by law, from allowing their sewage to discharge into rivers, and were required to provide that good drinking-water from a designated spring should be taken on board.

The above-mentioned "Denkschrift" gives an accurate account of the efficacy of these control stations, from which I have taken only the sum totals. In the months September to November there were—

	EXAMINED.		VESSELS DIS-INFECTED.	DISEASES DIAGNOSTICATED.	
	Vessels.	Persons.		Suspicious.	Cholera.
In the Elbe region........	57,108	205,954	32,851	11	108
In the Rhine region.......	37,078	185,542	21,144	2	5
In the Oder region (besides the harbor district of Stettin)	31,985	110,994	15,938	6	11
In the Weichsel region....	29,791	184,890	17,170	2	3
In 4 river regions.........	155,962	687,380	87,103	21	127

In the Danube region, also, the Bavarian government instituted a boat inspection under the direction of a State Commissioner.

Those found actually sick and likewise suspicious persons are to be isolated. The evacuations of patients are to be rendered innocuous by careful disinfection, and, when possible, afterward buried. For purposes of disinfection lime-water made from one part of burnt lime and four of water is at present preferred. This is very effective, if a quantity equal to the amount of the evacuation is added, thoroughly mixed by stirring, and allowed to stand for an hour. Chlorinated lime also added in the form of a powder may be employed. I prefer for disinfection of the stools ordinary or crude hydrochloric acid, or a 1% bichlorid of mercury solution.

The linen, the bed-clothes, and in general everything that may possibly have come in contact with the discharges are to be disinfected, the furniture, floor, and walls not expected. Whoever visits the sickroom must consider the possibility of his clothes and shoes coming in contact with the patient's dejecta. For physicians and nurses overcoats of linen similar to those worn where strict asepsis is required, which can be boiled without injury, are serviceable. According to the nature of the article, disinfection is to be carried out in different ways. Objects of little value had best be burned. After this the best means

of disinfection is thorough boiling in water, or, for articles that will not stand this, the thorough saturation with moist steam at a temperature of at least 100° C. Disinfection with hot air or with overheated dry steam is less certain, since the high temperature may not reach all parts of the object. A serviceable disinfecting apparatus, in which even larger objects like mattresses can be subjected to hot steaming, is an absolute necessity for every hospital. There are also portable disinfection apparatus. Wash- and bath-water may be disinfected by the addition of lime-water till a marked alkaline reaction is produced or by hypochlorite of calcium.

Besides these means of disinfection,—lime-water, hydrochloric acid, and mercury bichlorid,—others may be employed according to the article to be disinfected, such as a solution of soft soap (3 : 100), carbolic acid (5 : 100), lysol, creolin, mineral acids, alkalies, salts of metals, etc. For some articles several days' airing in the sun is of value. For the disinfection of rooms sulphur fumes or strong heat with subsequent thorough airing may be employed.

In 1867 I had the opportunity in Basel on the occasion of some cases being introduced of employing such measures against the further spreading of the disease. From Paris, where cholera then prevailed, two women came to Basel and there fell ill of cholera. At a meeting of the Board of Health, called without a moment's delay, the question was put if the cholera hospital, which was already arranged as a precautionary measure, should not be opened, but I held that this was unnecessary. Under the conviction that the discharges alone contained the specific cause, and that these could easily be made innocuous, I declared myself ready to receive both cases into the city hospital and to guarantee that a further spread of the disease would not take place. The then Medical Superintendent Officer of Health, Dr. DeWette, took it on himself to prevent a spread from the inn where the women had put up. The patients were placed in an isolated ward in the hospital. A trustworthy nurse, carefully controlled by myself and the assistant, stayed with them. The evacuations of the patients were received into porcelain vessels in which powdered sulphate of iron had been placed. Immediately after, hydrochloric acid was poured over them, and, together with the water used in washing the vessel, they were dumped into a recently excavated ditch in the garden, which after twenty-four hours was filled with earth and a new one dug. The vomited matters were treated in the same manner. If by accident a particle fell on the furniture or floor, it was covered at once with a handful of chlorinated lime. The soiled linen was put into a vessel filled with chlorid of zinc solution and thoroughly boiled the same day. One patient died, the other recovered. No further spread of the disease took place.

As regards all these measures, it should be laid down as a rule that in doubtful cases one should do too much rather than too little. Experience teaches that where only what is necessary is done, the result

is sometimes not fully attained, in that through a small and apparently insignificant omission on the part of the subordinate executive officials a break-down which is possibly of importance may arise in the precautionary measures. On this account many precautions are justified that may perhaps seem superfluous.

At the same time, all the notoriously injudicious regulations to which travelers even in recent years have been subjected should not be defended. Where, for instance, is the use of bringing a man into a room, fumigating him with chlorin vapor, or squirting him with other disinfectants before he is allowed to cross the border? The intestine of such a person, possibly containing cholera bacilli, is not to be disinfected in this way. At the most, the utility of such procedures consists in the fact that for a short time such people are characterized by the smell as coming from a cholera region or that these annoying regulations will disgust people with travel.

The second problem of general prophylaxis consists in lessening the predisposition of locality. The measures necessary for this, which are recognized by the Pettenkofer school as almost the only effective means of prophylaxis, are also generally considered as exceedingly important. As a matter of fact, the appearance of cholera has frequently given the signal for energetic improvements within the jurisdiction of Boards of Health and for regulations that prove useful in many other respects.

To lessen the local predisposition, von Pettenkofer's Y, we must keep two points especially before us: First, we must take care that the cholera bacilli, if they do find entrance, shall not find a culture-ground on which they may increase and develop into an infectious form; and, second, that if they do become infectious, they shall not pass over into man.

In relation to the first we can mention many circumstances that favor the multiplication of the bacilli outside the human body. Yet, for the present, bacteriology leaves us in the lurch as far as the exact conditions are concerned under which they become infectious, *i. e.*, acquire the necessary resistance and virulence. This gap, already referred to under the head of Etiology, can be bridged over in time only by direct experiences in relation to the predisposition of time and place. But at least the conjecture is justified that the same conditions which favor the multiplication of the organisms outside the body may also aid them in developing a greater resisting power and virulence.

With regard to the measures by which the local predisposition is lessened, we can refer to the etiology, and limit ourselves in this regard to the general aspect of the question. It is of the greatest importance that precautionary measures be taken before the danger becomes

urgent. And these precautions are especially advised since they protect not alone from cholera, but from a number of other epidemic diseases also. These measures consist principally in the removal of all rubbish and dirt from houses, courts, and streets, the keeping clean of cellar dwellings, attention to judicious arrangements for the disposal of sewage, especially in the low-lying parts of a town, and the improvement of sanitary conditions in habitations both in the country and in cities. If danger of importation of the disease threatens,—that is, if cholera breaks out in a place with which trade exists,—all these things are to be looked to with the greatest diligence, and if anything has been omitted, the omission is to be made good at once, especially if the season is favorable for an epidemic spread of the disease. If privy pits exist they should be emptied and water-closets or latrines should be thoroughly disinfected.

In Basel in 1867, when cholera threatened from several directions, among other measures, prophylactic disinfection was carried out with great consistency. The police were instructed to disinfect with sulphate of iron and carbolic acid all the latrines and water-closets in the hotels, restaurants, boarding- and lodging-houses, schools, and railway stations daily, and in all private houses once or twice weekly, without concerning themselves whether or not the same was done by the owners. In spite of continued traffic with cholera districts, no case of cholera, with the exception of those introduced from outside, appeared in Basel.

For disinfection of latrines and water-closets, sulphate of iron (copperas) was in former years especially employed. It is true that this is less bactericidal than many other metallic salts, but, besides the advantage of cheapness, it possesses a slowly oxidizing effect, in that the oxid of iron arising from the absorption of oxygen keeps on transferring oxygen to the organic matter. Recently lime-water in large quantities and chlorinated lime have been used. In many places it is of some, if only secondary, importance to know that the value of the manure as a fertilizer is not thereby impaired. Crude hydrochloric acid and all the other mineral acids are likewise effective disinfectants.

All these measures, and especially disinfection also, are chiefly effective when they are employed as prophylactics; yet if an epidemic occurs, they are to be continued as long as it lasts. This does not apply to the cleaning out of latrines and cesspools, which is useful only as a prophylactic, and must later be avoided on account of the danger of dissemination.

Among the preparations to be made previous to the appearance of an epidemic is the formation of a committee to carry out disinfection; for the procuring of adequate disinfecting apparatus and the estab-

lishment of cholera hospitals, for which barracks are usually very suitable; and, lastly, for providing that a sufficient number of trained nurses are ready at hand in case of emergency.

The opinion as to the measures to be taken in order to prevent the introduction of infectious cholera bacilli, when present, into the human body, depends partly on the conception one has formed as to the usual mode of infection. Von Pettenkofer's dogma, that infection cannot occur through the drinking-water, has been so forcibly controverted by the severe experience of later years that no amount of rhetoric could again create faith in it. We shall therefore place in the front rank the provision of a good drinking-water that has not been exposed to contamination. How this is to be obtained is one of the most important and difficult problems which the Board of Health is called upon to solve, and it cannot be answered in general because it must of necessity depend on the special local conditions. It need only be mentioned here that where filtered water is used and the harmlessness of the drinking-water is dependent on the trustworthiness of the filtration, there is but little security, inasmuch as the best filtration plant may prove at times imperfect, and for the control of its bacteriology continuous bacteriologic examinations are necessary. At the time of an epidemic all sorts of suspicious water-supplies or wells are to be so isolated that it will be impossible to make use of them. At the same time, however, the procuring of good drinking-water must not be forgotten. When considering individual prophylaxis, we will return again to the question of drinking-water.

Several investigators have been led by theoretic considerations, and, further, by the experiences of late years, to the opinion that cholera epidemics in almost all cases spread through the drinking-water. When discussing the etiology of the disease, I have endeavored to demonstrate that this view was one-sided, and that probably there were still other ways of infection; in fact, that infection even through the air was not a rarity. How such may best be avoided will be discussed in part under individual prophylaxis. In reference to this, here is one set of regulations, as carried out in Basel during the epidemic of 1855, which I heartily recommended in the epidemic of Heilbronn in 1873, and which was there carried out with good success: to thoroughly clear all houses in which cases of sickness existed, in order to prevent them acting as foci of infection, to remove the inhabitants thereof to other shelter while the epidemic lasted, and, further, to keep a careful supervision over them. All cholera cases, as far as it is possible with-

out force, are to be brought to special hospitals, yet the transport of them a long distance is to be avoided.

If a cholera epidemic already exists, or even but threatens, it is best to put all the regulations into the hands of a committee composed of physicians and intelligent laymen, and endow them with full powers. The police should be employed only in aiding the enforcement of the measures. This committee should, among other things, make it their business to instruct the public on points in keeping with the regulations. Regular and trustworthy official reports on the state of the epidemic serve to inspire and maintain confidence, while all secrecy has a bad effect. Of great importance is the strict enforcement of compulsory notification, not alone of the actual cases, but even of the suspicious ones, for which not only the physicians, but also the house-owners should be held responsible.

The different circulars issued from the office of the German Chancellor in regard to the regulations against cholera may be found among other places in the "Deutsche Vierteljahrsschrift für öffentliche Gesundheitspflege."

INDIVIDUAL PROPHYLAXIS.

Whoever has no business in an infected or threatened district had better remain away or leave it. Whoever remains, let him avoid as much as possible the houses, and especially the latrines and water-closets that are or may be sources of infection. Let every one endeavor to prevent the origin of a focus in his own district by attention to his dwelling, thorough disinfection of the water-closets, regular removal of all refuse matter, and, above all, by painstaking cleanliness. Water used for drinking purposes which is in the least suspicious must be boiled before it is drunk, and even before it is employed in washing food utensils. Unboiled milk also is to be avoided, likewise ice the origin of which is not thoroughly known. Genuine mineral waters are allowable. Food must be protected as much as possible from flies and other insects. Fresh fruit, and especially all uncooked food, had best be eschewed. In general, it is advisable to change the previous mode of living as little as possible, and only to be somewhat more careful to avoid everything that might cause digestive disturbances, especially diarrhea. Remedies having a prophylactic effect, which are so often recommended, have not justified their use. That copious quantities of alcoholic beverages, especially red wine, protect against cholera is a gross delusion. Moderate amounts are harmless for those accustomed to them, but all excess is dangerous. Generally speaking, excesses of every kind are to be avoided. Precautions are to be taken against

chills and other harmful influences. Above all, the individual should accustom himself at the time of an epidemic to regard every diarrhea as a dangerous disease requiring the most careful treatment.

A person who in the performance of his duty is brought in contact with cholera patients or their dead bodies is, if he careful, in no greater danger than other people. The evacuations and intestinal contents alone are dangerous, and these only when introduced into the mouth. Therefore such a person need only avoid eating in the sickroom, and if he has come into contact with the sick or dead, he should take care afterward to thoroughly disinfect his hands, which is most readily done by soap and water and a bichlorid of mercury solution (1:1000). It must not be forgotten that infectious particles may adhere to the clothes.

In regard to prophylactic inoculation, as carried out by Ferrán in Spain, and most recently in large numbers of cases by Haffkine in India, no definite conclusion can be drawn at present. Yet even if the results prove favorable, the general employment of the method should not be recommended; at the most, it would be applicable only to individual persons who as the consequence of particular circumstances stood in very great danger of infection. The experiments on the prophylactic effect of the substances designated anticholerine and cholera antitoxin are likewise inconclusive.

TREATMENT OF THE CHOLERA DIARRHEA.

The cholera diarrhea is the stage in the disease in which it is amenable to treatment and in which an early judicious treatment leads to a successful issue in the great majority of cases.

If at the time of an epidemic any one is attacked with diarrhea, without concerning himself as to whether it is actually cholera or only a simple disturbance possibly the result of dietetic errors, he should regard it as a serious disorder, all the more so if he feels otherwise well and experiences no pain. Such a person must take to bed, and by warm coverings, and peppermint tea or other warm drink, endeavor to produce a mild perspiration. Poultices applied over the abdomen may serve as an aid in the treatment. Opium is to be at once exhibited in small but frequently repeated doses. For the time being, nourishment is to be limited to barley-water or oatmeal-water, tea, and a little red wine.

Since the result of treatment is the surer the earlier it is begun, it is advisable at the time of an epidemic to instruct the public in the great

importance of diarrhea and the necessity of its careful treatment. It has proved very satisfactory in many places to have physicians take it on themselves to visit regularly from house to house and treat at once every person becoming ill. It is further advisable that opium in a form in which it can be employed with advantage before the arrival of the physician should be kept in every house for the immediate treatment of a perhaps commencing diarrhea. The best preparation for this purpose is a diluted tincture; for instance, in the form of the Lorenz's cholera drops now so long in use:

R. Tinct. opii crocatæ 6.0
    Vini ipecac................................... 4.0
    Tinct. valerian. æther........................12.0
    Ol. menth. piper.............................. 1.0.   M.
Sig.—15 to 25 drops every half-hour.

A corresponding powder answers the same purpose:

R. Opii......................................0.02 (2 ctgm.)
    Rad. ipecac. pulv............................0.03
    Sacchar. ....0.05.
M. f. p. Dentur tales doses No. 5.
Sig.—One powder every half-hour.

Or the following mixture has a good effect in the treatment of the diarrhea:

R. Sodii bicarbon................................ 5.0
    Tinct. opii simplicis ⎫ ....āā 1.5
    Tinct. nucis vomicæ ⎭
    Aq. menth. piper. 180.0
    Sacchar. .... 10.0.   M.
Sig.—One teaspoonful every half-hour.

This treatment frequently shows rapid results if begun early enough. But in individual cases, and especially when the treatment is commenced late, the diarrhea continues or even becomes worse. The preferable treatment now is a few doses of calomel, about 0.3 or 0.5 every one to two hours until the appearance of profuse green calomel stools. Then opium is taken up again. Under special circumstances the administration of calomel may require repetition later on.

This treatment of cholera diarrhea has proved successful in every place, and continues to be employed by the majority of practitioners. Recently, chiefly on the ground of theoretic speculation in relation to the behavior of the bacilli and their toxins, scruples have been raised against it. It has been asserted that if the intestine is set at rest by opium, then surely an apt opportunity is offered for the bacilli contained therein to multiply and elaborate their toxin at leisure. Long

before the discovery of the micro-organisms repeated doses of castor oil, neutral salts, and other purgatives, and even emetics, were employed at the commencement of the disease in order to rid the intestine of supposed injurious substances. But calomel has always been returned to in either purgative or long-continued small doses of 0.05 to 0.1. And since there was reason to believe in the bactericidal action of the calomel, the hope was raised that by the employment of other more powerful germicides greater results might be obtained, perhaps even the cure of an outspoken attack. All the disinfectants that could be employed internally were tried, as, for instance, chlorin-water, mineral acids, other mercurial combinations, salts of copper, bismuth subnitrate, arsenic, iodin, iodoform, chloroform, oil of turpentine, creosote, benzol, creolin, cresol, resorcin, thymol, pyoktanin, skatol, benzoic acid, lactic acid, salicylic acid and its salts, salol, tribromsalol-bismuth and tribromphenol-bismuth, caffein, sodium salicylate, cocain, quinin, veratrin, strychnin, etc. So far, none of these remedies have shown satisfactory results, and this is not remarkable if we reflect that they meet in the intestine large quantities of fluid, which so dilutes them that they become almost ineffectual. Moreover, it is possible that the bacilli have already penetrated too deeply into the glands and mucous membrane for the disinfectants to be able to reach them. Yet further attempts are being continually made with different kinds of specific treatment, and, although past experience should warn us against immoderate expectations, yet the hope is by no means to be abandoned that possibly further investigation will bring to light a specific that will act in cholera like quinin in malaria, mercury in syphilis, or salicylic acid in acute articular rheumatism. Perhaps, too, the future may open the way to a curative serum as successful as Behring's in diphtheria, even though neither the anticholerine of Klebs nor the cholera antitoxin of Fedoroff or of Ransom-Behring should prove to be a remedy of that kind.

Among the more recent measures must be mentioned the tannin-enteroclysis of Cantani, which has been frequently found useful in obstinate cases of cholera diarrhea and cholerine, and also in the beginning of the actual attack. It is to be employed especially in cases of obstinate vomiting that are not affected by opium. One or two liters of a 1% tannin solution in previously boiled water at a temperature of 39° to 40° C. is allowed to flow into the large intestine, and this is repeated several times daily. The good effect commonly observed is due in part to the introduction of heat, and perhaps, too, to the absorption of fluid from the large intestine; but sometimes the ileocecal

valve may be passed, so that a direct action on the diseased small intestine results.

Cantani believed that the fluid passed the ileocecal valve in most, if not in all, cases as a result less of the pressure of the column of water than on account of the induced antiperistaltic movements in the intestine.

Von Genersich lately expressed his belief that the ileocecal valve could be passed in every case if he injected large amounts of liquid under a pressure represented by a water column of 80 to 100 cm. When about 9 liters are poured in, the fluid begins to flow from the mouth, and by this "diaclysm" the entire small intestine and the stomach may be washed out. He commonly employs in cholera a 0.1 to 0.2% tannin solution, but he is of opinion that the good results are due principally to the flushing of the intestinal canal, and that therefore a 0.75% common salt solution or other indifferent fluid would act as well. These statements are sufficient to induce a trial of Cantani's enteroclysis with large amounts of water, in as far as it can be done without too great disturbance to the patient. Yet the tannin solution should be made correspondingly weaker.

A daring operator has already experimented on the treatment of cholera surgically. He laid open the abdomen, cut through the bowel, and then with hollow sounds introduced above and below he washed out the intestine with a disinfecting fluid. The results are described as "negative."

TREATMENT OF THE CHOLERA ATTACK.

So long as no vomiting exists, we may hope to effect an improvement in the intestinal condition by opium and calomel. A few large doses of the latter are sometimes sufficient to lessen decidedly the diarrhea. In addition, every effort must be made to induce moderate diaphoresis. If vomiting is present, it must be combated by small quantities of brandy, champagne, mulled wine, whisky, tablespoonfuls of hot coffee or tea, by a mustard plaster on the abdomen, or, finally, by a subcutaneous injection of morphin. In India the subcutaneous injection of watery extracts of opium is also often employed. Should these means fail, and, still more, should the vomiting obstinately continue, so that everything introduced into the stomach is thrown off, a further exhibition of fluid or drugs by the mouth is useless, and it is only possible to try to lessen the thirst by swallowing or holding in the mouth bits of ice. Sometimes small enemata of chamomile tea with a few drops of tincture of opium may be retained and absorbed; if so, they are to be frequently repeated, though usually they are quickly evacuated with large quantities of intestinal contents. The tannin-enteroclysis of Cantani may then be employed. Sometimes the vomiting becomes less after washing out the stomach with a 0.5% salt solution.

If the skin is cool and the pulse weak, external heat is indicated in order to restore the peripheral circulation. This is best accomplished

by warm or hot baths. Yet these must be given with caution. Though individual observers have seen no good effect from the hot baths, this is partly due to the fact that they were often used too ener- getically, in that the bath at the beginning was too hot and too little attention was paid to the existing general condition and the tempera- ture of the skin of the patient.

The temperature of the bath at the beginning should be at most 35° C. (95° F.), and should be very gradually increased by the addition of hot water to 40° C. (104° F.). The duration of the bath depends on the condition of the patient during it. It may usually be continued for fifteen minutes, and often for a considerably longer time. Afterward the patient is simply wrapped in a linen cloth, then in blankets and covered with a feather bed. Frequently after this sweating occurs, especially when one of the methods of introducing fluid which we will mention later be employed. Steam and hot-air baths are less to be recommended, since in them it is not possible to regulate sufficiently the temperature to the condition of the skin.

The greater the lack of water in the body and the thicker the blood, the more desirable does it become to introduce some watery fluid. Since the ordinary channels for the introduction of fluid, through the stomach and intestine, are closed, new ones must be sought. Fre- quently by enteroclysis a certain amount of absorption may be brought about. In the hope of inducing absorption through the bladder, Piorry (1849), and more recently Barth and Mettenheimer, recom- mended injections into that viscus. The procedure promised but little result, and is entirely futile. Injections into the peritoneal or pleural cavity, which have been recommended, should absolutely be omitted. Much more effective is the introduction of fluid subcutaneously or by transfusion into the veins.

Hypodermoclysis, or the subcutaneous injection of large amounts of fluid, was proposed by Cantani as early as 1865, and later by others, and the plan was in isolated cases attempted. The method was again brought under notice by Samuel (1883), and since 1884 has been car- ried out by different physicians in a large number of cases. It was employed extensively in the Hamburg epidemic of 1892. The solu- tion used consists of 6 gm. of sodium chlorid, or, on account of the lessened alkalinity of the blood, 4 gm. of sodium chlorid, with 3 gm. of sodium carbonate to 1 liter of water which has been sterilized by boil- ing and cooled to 40° or 38° C. (104° or 100.4° F.). A hollow needle is introduced under aseptic precautions and half a liter is allowed to flow under the skin in several places simultaneously or at one after

another. The preferable regions are into the abdominal wall, the thigh, or the buttocks. The region of the neck is to be avoided on account of the consequent swelling. The first effect is commonly good, in that the pulse becomes stronger and the general condition is decidedly improved. Unfortunately, in patients who have already passed into the asphyxial condition this effect is only transitory, and even by repetition of the subcutaneous injections the improvement in many cases cannot be made lasting.

Still more striking are the first effects of intravenous transfusion. It was recommended as early as the first European cholera epidemic (Hermann), and was frequently employed in the thirties (1831–1840), principally by English physicians. Later, and especially in the Hamburg epidemic of 1892, the treatment was taken up again. Schede describes the immediate effects of intravenous transfusion as follows: "You have before you a man cyanosed, ice-cold, entirely pulseless, with half-open eyes sunk deep in the sockets, exhibiting no reflex of the cornea, which may be already dried up, unconscious and without feeling. You lay open a vein, but the pain of the cut calls forth absolutely no reaction. The cannula is fastened into the vessel and the warm solution (we prefer it, 40° to 42° C.) poured in. From 200 to 300 gm. have scarcely been introduced when the effect begins to show itself, and before the ordinary amount of 1000 to 1500 gm. is reached the picture is entirely changed. The lips are again cherry-red, the cheeks of healthy color, the eye regains its luster, sensation returns, the blood streams through the arteries with a full strong pulse, the breathing becomes deep and quiet and is accompanied by a certain often very evident feeling of comfort, which patients who previously were not entirely apathetic boastingly make very evident, consciousness is again present, the patient shows signs of intelligence, knows his name, etc." In individual cases the urinary excretion is restored by the infusion, but in the majority this does not happen, in spite of the injection of copious quantities of fluid. Moreover, the effect is frequently only transitory, and usually no lasting result follows the repetition of the transfusion. Possibly more success might be attained if, as has been proposed (Samter), a venesection in another part of the body be practised simultaneously with the transfusion.

Transfusion into the arteries seems to have no advantage over that into the veins, and it is, moreover, more difficult to carry out.

The results of subcutaneous and intravenous transfusions as extensively carried out in 1892 in the Hamburg hospitals have been reported by Sick, Hager, Reiche and Wilkens, and Lauenstein.

From the communication of Sick we learn that intravenous transfusion was done in the different Hamburg hospitals on 1659 patients, of whom 382 recovered and 1277 died. This gives a mortality of almost 77%, which appears at first sight very unfavorable; but considering the condition of the patients, most of whom were already in the stage of asphyxia, it may perhaps be better than it would have been without the transfusion.

Somewhat more favorable is Hager's report of 967 cases treated in the old hospital, sometimes by intravenous, sometimes by subcutaneous injections, and again by both. Of these, 291 recovered and 676 died. The mortality was therefore not quite 70%. Of 345 cases treated by intravenous injections alone, 97 recovered and 248 died, a mortality of 72%. Of 494 treated by subcutaneous injections alone, 181 recovered and 313 died, a mortality of 63.4%. It appears, therefore, that although the immediate result is more marked with intravenous injections, in general subcutaneous injections deserve the preference.

Lauenstein sometimes observed after intravenous injections a chill with a transitory rise of temperature, which he is inclined to attribute to the fact that the salt solution was not absolutely sterile.

Galliard, in Paris, had among 143 cases *in extremis* treated by intravenous transfusions, 25 recoveries, and he is convinced that without this treatment these, too, would have succumbed.

Keppler, in Venice, reports especially favorable results with subcutaneous injections. He employed a solution of common salt to which 1% absolute alcohol was added. He states that he experimented only on very severe cases abandoned as hopeless by the physicians. Of these, 44.4% recovered. Unfortunately, the number of cases treated is not stated.

Cavagnis treated in 1886 in Venice, 36 patients in the algid stage with subcutaneous injections. Of these, 14 recovered, a mortality somewhat under that of this epidemic, which was 65.5%.

The results in general of subcutaneous and intravenous transfusions are not so favorable as was anticipated, and many physicians whose expectations were raised to the highest pitch were utterly disappointed when they were not fulfilled. Moreover, these experiences had no little influence in discrediting the opinion that the symptoms and progress of cholera were essentially due to the loss of water. Yet, on the contrary, the immediate and decided effect of the transfusions ought to demonstrate how greatly responsible for the symptoms the loss of water is. That the favorable effect is frequently short lived, and that a repetition of the transfusion usually fails to save the patient and that he should succumb to failure of the heart with a return of the collapse, or later in the condition of typhoid, is not remarkable even if we regard the loss of water and heart weakness as the causes of the symptoms. The idea is too childish to believe that it would be possible to compensate forthwith for all the mischief on the mere restoration of the water. The principle "*cessante causâ cessat effectus*" is applicable only in jurisprudence, not in biology or medicine. Experimen-

tally, it can be shown that, if the blood supply of the kidneys is cut off for a time, its restoration is by no means sufficient to bring about the normal condition; on the contrary, it is then that the degenerative changes begin to show themselves. And so it is without surprise that we see in most severe cases of cholera after restoration of the fluid, and even re-establishment of cardiac activity, the kidney function not at once return to normal. Moreover, all the other organs behave like the kidneys, and the heart especially is not so easily made capable of lasting activity. Many organs are so severely injured by the lack of water and the depression of the circulation that they never entirely recover even after removal of the cause. Perhaps the introduction of water would be more favorable the earlier it was done, since then the results of the loss of water might be avoided.

In addition to the other treatment, if heart failure threatens, the subcutaneous injection of liniment of camphor, ether, and such like is to be employed. For the violent muscular cramps, when warm baths have no influence, an injection of morphin will be found effective. Diaphoretic measures, especially warm baths with the subsequent pack, should be continued. These have more effect after profuse transfusions. To keep up the peripheral circulation the extremities should be kept warm, the skin rubbed, and mustard plasters or other counter-irritants employed.

When the diarrhea ceases and absorption from the intestine is re-established, the heart activity can be kept up by red wine, mulled wine. hot whisky-punch and other spirituous liquors, or by ether, preparations of ammonia, strong tea or coffee, camphor, and musk. Then, too, the loss of water may be compensated for by the cautious administration of weak tea or coffee, bouillon, wine, mineral waters, and especially by repeated small clysters of chamomile tea with a little tincture of opium.

TREATMENT OF THE COMPLICATIONS.

In that most frequent of the complications, cholera typhoid, the special cause of the condition is to be diligently sought for. In the less severe cases in which the typhoid condition is to be regarded merely as the result of slight cerebral weakness, or of a simple reactionary fever, expectant treatment is commonly sufficient. When particular local diseases underlie the condition, these are to be treated according to their peculiarities. If there is reason to attribute the typhoid state to uremia or toxemia, the urinary excretion is before all else to be promoted. For this purpose, diuretics that irritate the kidneys are to be

avoided, but saline diuretics, especially potassium acetate, may be employed without hesitation. The urinary secretion increases most profusely under the introduction of large quantities of water. The patients should be persuaded to drink seltzer or other weak saline or saline-alkaline mineral water, to which can be added hot milk, in order that the mixture may be lukewarm, yet always in small quantities at a time. When the stomach refuses, the same object may be attained by frequently repeated small enemata of chamomile tea with a little tincture of opium.

If an inclination to diarrhea continues, the patient should be kept in bed, poultices applied over the abdomen, and a strict diet enforced. In any event the nourishment in convalescence should be liquid, consisting especially of not too strong bouillon soups, with strained barley or oatmeal groats. Milk must be boiled in all cases, and since it is often borne badly when undiluted, it may be mixed with weak coffee or tea or seltzer water. Solid food is to be avoided at the beginning; later on, when improvement begins, a little well-baked white bread or rusk may be allowed. Butcher's meats should be permitted only after complete recovery. When the diarrhea is more or less obstinate, opium in small repeated doses must be exhibited. When constipation alternates with the diarrhea, a gentle and systematic treatment with Carlsbad water will be found effectual.

Similar procedures are to be advised in cases of diphtheritic or ulcerative processes in the intestine; and, in addition, injections of 1% tannin solutions or other weakly astringent fluids are to be employed.

If during convalescence symptoms of heart failure appear, they are to be combated by red wine, mulled wine, whisky, strong tea or coffee, and in cases of necessity by subcutaneous injections of camphor liniment.

CHOLERA NOSTRAS.

UNDER the name of cholera nostras we include all attacks of illness which simulate cholera Asiatica, or its mild forms cholerine and cholera diarrhea, but which are not produced by the specific microbe of cholera Asiatica. It results from this somewhat negative definition of the disease that the term cholera nostras does not indicate a specific and definite disease, but that under this name are included many diseased conditions, which agree only in their symptomatology, but may be quite different in their etiology. It is to be expected that further investigation will lead to the discrimination of the different maladies which have been hitherto grouped together as cholera nostras according to their particular etiology. Even now we can distinguish the fermentation diarrhea of very young children, which should be described as cholera infantum, from cholera nostras, and pass it by without further consideration.

Cholera nostras is seen in all countries and at all seasons. What the physicians of antiquity and of later times down to 1817 described as cholera, was cholera nostras; though it was not always sufficiently differentiated by them from other diseases of the intestinal canal, especially dysentery.

ETIOLOGY.

IT is in the highest degree probable that infection underlies at least many cases of cholera nostras. Since Finkler and Prior found in cases of cholera nostras a comma bacillus having a certain resemblance to that of cholera Asiatica, we may assume that at least some of the cases have a specific etiology, and that the disease, like cholera Asiatica, depends on the introduction of a specific micro-organism. Under these circumstances cholera nostras would stand in relation to cholera Asiatica as varicella to variola, rubella to measles, epidemic icterus to yellow fever, simple gastric fever to typhoid. It would represent with regard to Asiatic cholera what I have designated as its weaker parallel form. More recently, too, bacilli have been occasionally found by individual observers in cholera nostras that corresponded to those of Finkler and Prior, yet in the very great majority of cases these bacilli

have been absent.   As a rule, in the evacuations and intestinal contents in cholera nostras only such micro-organisms are found as are present in the healthy intestine, though frequently one or other kind predominates in a striking manner, most commonly the Bacterium coli commune (Escherich).   In other cases have been found especially numerous streptococci or staphylococci, sometimes also bacilli resembling the subtilis; further, the proteus forms, and, finally, in exceptional cases microbes that were distinguished only with difficulty from the bacilli of cholera Asiatica.   Less attention has been given to the larger infusoria, as Megastoma, Trichomonas, Cercomonas, Balantidium, and Amœba, which are found in individual cases of both acute and chronic diarrheas.

The relation of the schizomycetes (Spaltpilze) found in the stools and intestine to the disease may be regarded in different ways.   It is conceivable that a disturbance of function of the intestine or a change in its contents may lead to an unwonted multiplication of one or other of the micro-organisms present in it; in other words, the disease of the intestine or the change in its contents may be primary, the increase in micro-organisms merely secondary.   It is possible, too, that the disease may be originally produced through the introduction of special schizomycetes; and in this connection we may either think of micro-organisms which were not previously forthcoming in the intestine, or also of the possibility of the usual intestinal microbic parasites assuming an exceptionally virulent form.   The great variability of, for instance, the Bacterium coli commune lends countenance to this last-named possibility.   Finally, the relation of the two may be complex—namely, some injury or other may produce a disturbance in the intestine; this results in so extraordinary a development of micro-organisms or in their becoming so virulent that they in their turn cause further disturbances.   In which of these possibilities lies the true explanation, or in what cases the different explanations may be applicable, is left for future investigation to decide.   Yet one view based on the variability of the schizomycetes, and which has recently been frequently suggested, especially by French observers, can be absolutely denied—namely, the opinion that the variability may be so wide as to allow, under particular circumstances, cholera nostras to develop into cholera Asiatica, by the conversion of the Bacterium coli or some other ordinary intestinal micro-organism into the true comma bacillus.   As far as historic knowledge extends, we see cholera nostras at all times in all countries, but we have never even heard of a case of it becoming cholera Asiatica in any country.

Among the lesions that may lead to cholera nostras are, first, grave dietetic errors. Either simple overloading of the stomach or the ingestion of unsuitable food and drink, such as contaminated drinking-water, stale beer, food-stuffs, spoiled or undergoing decomposition, may be the cause of an attack. Very many cases also of poisoning by meat or vegetables or through non-edible mushrooms, shell-fish, fish, cheese, etc., run their course with the symptoms of cholera nostras. A further cause is "catching cold," especially in the abdomen, or over-indulgence in cold drinks or ice. The inhalation of foul gases has been reckoned among the causes, and even violent emotions induced by anxiety or fright. Finally, in many cases no particular exciting or predisposing cause can be demonstrated.

Cholera nostras is seen most frequently at midsummer and toward autumn. Only exceptionally does it occur at other seasons. It is apparently favored, like all bacterial vegetation, by a high external temperature. Sometimes the cases are isolated, so that one may correctly speak of cholera sporadica, but frequently they appear in numbers corresponding to an endemic or epidemic prevalence. If in one family or in one house several cases occur, it is most likely that the same untoward influences affected the different people; and if within a certain time many cases appear in an entire city or in a large portion of a country, they may be safely attributed in part at least to conditions that are the same for such regions, as weather and temperature. Moreover, observations have apparently shown that the disease in one individual may act as a focus for further spread, so that the possibility of direct or indirect contagion must be considered. Yet the epidemics of cholera nostras never become by any means so widely spread as those of cholera Asiatica.

It has frequently happened that at a given place a number of cases of vomiting and diarrhea preceded an outbreak of Asiatic cholera. Special emphasis has been more than once laid on this coincidence; in fact, it has been taken for a confirmation of the opinion that cholera Asiatica may arise autochthonously or may develop from ordinary cholera nostras. Still, this coincidence is really by no means striking. The same local conditions, the same temperature and weather phenomena, the same individual circumstances, that favor cholera Asiatica are necessary for cholera nostras; it can therefore be premised that where there is much cholera nostras, Asiatic cholera, if introduced, will find a suitable soil. Moreover, it is to be considered that in large cities numerous cases of cholera nostras occur almost every summer, yet it is only when cholera Asiatica follows that these are mentioned and

pointed out as the precursors of the more serious malady.   And, on the other hand, numerous epidemics of cholera Asiatica have been observed which have had no such forerunners.

Cholera nostras occurs at every age and with practically no predilection for sex.   A certain predisposition to the disease seems to be imposed by all sorts of digestive disturbances.

SYMPTOMATOLOGY.

THE symptoms of cholera nostras correspond generally to those of cholerine or cholera diarrhea.   Ushered in by such prodromata as nausea, rumbling and pain in the abdomen, gastric discomfort, but in other cases absolutely without any such forerunners, there is a sudden attack of very profuse diarrhea with or without abdominal pain.   The evacuations may be more or less frequent, are watery, and usually remain bile-stained.   Frequently there is vomiting also, and this is often the first and continues to be the most important symptom.   The contents of the stomach are first vomited, then a bile-stained fluid follows.   Occasionally everything ingested is at once thrown off. The pulse is weak and frequent, the hands and feet show a tendency to become cold.   The patient feels prostrated, is pale, but apart from intense thirst has no especial complaint.   Yet in other cases there is more or less pain, or a decided feeling of weight, in the gastric region. The abdomen is sometimes distended (meteorism); in other cases it is flat and retracted, and frequently sensitive to pressure.   The disease usually terminates favorably.   After a few hours or several days the vomiting ceases, the evacuations become less frequent, and the patient gradually recovers.

Besides these mild cases that constitute the overwhelming majority, there are severe forms in which the symptoms correspond so closely at every stage to frank Asiatic cholera that a bacteriologic examination furnishes the only means of a differential diagnosis.   The copious evacuations that may eventually become colorless and assume the appearance of "rice-water" stools produce a similar impoverishment of water, with its results.   The urine becomes scanty or even suppressed, vox cholerica is apparent, and cramps in the calves occur. The cheeks fall in, the eyes lie deep in the sockets, the extremities become cold and cyanotic, the pinched-up skin remains wrinkled.   The heart may become exceedingly feeble and an outspoken condition of

asphyxia may develop. In these severe cases a fatal termination is not rare. If after such an attack in which a very marked diminution in the quantity of urine, or even anuria, occurs, the patient recovers, the urine remains for a time albuminous. Moreover, reactionary symptoms, complications, and even indications of a typhoid condition may set in.

ANATOMIC CHANGES.

WHEN a patient has succumbed to a severe attack of cholera nostras, the postmortem finding to the naked eye does not differ from that of cholera Asiatica. The skin is similarly shrunken, rigor mortis is strongly marked. There are indications of cyanosis. The subcutaneous areolar tissue and muscles are very dry, the serous membranes show a similar glassy tenacious exudate. The small intestine has the same reddish color; the stomach and bowel may be more or less filled with fluid and may exhibit ecchymoses here and there. The solitary follicles and Peyer's patches are often enlarged, and sometimes ulcerated. The kidneys show the early indications of degeneration, the bladder is usually empty. The pericardium contains no fluid. The blood is thick.

DIAGNOSIS.

A CERTAIN differential diagnosis of cholera nostras from cholera Asiatica cannot be made from either the symptoms or the simple postmortem lesions. We may say that on an average the cases of cholera nostras are much milder and less dangerous, and there is not the same inclination to epidemic extension, yet these points are insufficient to act as a basis of diagnosis in individual cases which when mild correspond to cholerine or cholera diarrhea, and when severe conduct themselves like true cholera. True, in the great majority of cases the diagnosis presents no difficulty, but this is dependent on the fact that they occur at a time when cholera Asiatica is not near at hand, and that they can therefore be at once recognized as cholera nostras. Yet if an epidemic of cholera Asiatica exists, or if, even though the outbreak is far away, there is the slightest possibility of the introduction of the disease, then all other characteristics fail and a differential diagnosis can be made only by a thorough bacteriologic investigation.

The same is true for the discrimination between cholera nostras and

ordinary intoxications, as was mentioned under the heading Diagnosis of Asiatic Cholera. A sharp distinction in regard to poisoning by different kinds of decomposed food-stuffs is not possible, yet in individual cases the careful investigation of surrounding circumstances frequently leads to the discovery of such a cause for the illness. Above all, it must not be forgotten that the term cholera nostras serves as a generic name for a variety of conditions that are etiologically very different. Sometimes a careful history of the attack and a closer investigation will reveal the presence of definite alimentary disturbances or other causes. Again, a bacteriologic examination may show such large numbers of certain micro-organisms in the stools that we can with greater or less probability recognize the disease from them. Finally, in many cases we must give up an accurate etiologic classification and satisfy ourselves with the bare diagnosis of cholera nostras.

PROGNOSIS.

ORDINARILY the prognosis is favorable, even when threatening symptoms are present. Yet in old people, in young children, and in already feeble persons a moderately severe attack may prove fatal. Moreover, a patient who does not take care of himself, but remains on his feet and keeps going about, may succumb to a sudden anemia of the brain or paralysis of the heart; or by neglect or improper management a mild case may become serious and dangerous. In the rare very severe cases the prognosis is much more doubtful, yet in these the symptoms have not, as a rule, so serious a signification as in cholera Asiatica.

Although, generally speaking, it is the exception for a patient to succumb to cholera nostras, epidemics sometimes occur with a comparatively high mortality. For instance, in 1893–1895, of 174 cases investigated by the Hygienic Institute of Breslau, 70 died, a mortality of 40% (Gotschlich). In a small epidemic observed by Carp in Wesel, of 6 cases 5 died.

TREATMENT.

THE treatment for ordinary cases is the same as that for cholera diarrhea. In addition to rest in bed and strict diet, the chief remedy is opium, which, exhibited in small and frequently repeated doses, usually gives quick results. Even the vomiting soon yields to repeated

doses of 5 drops of the tincture of opium. In cases where the vomiting was so violent and obstinate that nothing could be taken by the mouth, I have achieved excellent results from repeated small enemata of 80 to 100 gm. of chamomile tea and 5 drops of the tincture of opium. In addition, mild sweating should be induced by warm covering and hot drinks (peppermint tea, etc.). If considerable abdominal pain is present, large poultices may be applied. If the extremities become cold owing to the depressed circulation, warm baths should be given or friction applied to the skin, together with strong stimulants or wine, hot coffee or tea internally, or, when necessary, an injection of oleum camphoratum. In case the diarrhea remains obstinate, it may be well to administer several doses of calomel of 0.3 or 0.5 gm. every two hours until the appearance of green calomel stools. As for the rest, all excessive treatment and all violent meddling should be avoided.

The severe cases are to be treated similarly to Asiatic cholera. In these, tannin-enteroclysis and the subcutaneous injection of large quantities of fluid may be found useful.

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TO LITERATURE ON CHOLERA ASIATICA AND CHOLERA NOSTRAS.

THE literature on cholera is extraordinarily voluminous and profuse in detail. In the carefully compiled and complete Index Catalogue of the Library of the Surgeon-General's Office at Washington, which, after all, contains only the books and articles belonging to the library, there are in volume III (1882) on 151 folio pages about 10,000 references to different articles on cholera. For the literature before 1882 the student is referred to this rich index. A practical review of the still more voluminous literature of subsequent years is given in the "Jahresbericht" of Virchow and Hirsch. In the following references I have limited myself to culling from the early and recent literature the greatest part of the works which I have made use of or to which I have called attention in my treatise.

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    42.

ERYSIPELAS

AND

ERYSIPELOID.

BY

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ERYSIPELAS AND ERYSIPELOID.

ERYSIPELAS.

ERYSIPELAS is an acute, febrile, infectious disease which is characterized by a peculiar inflammatory redness and swelling of the skin or of the mucous membranes adjacent to the natural orifices of the body. This redness and swelling are always sharply circumscribed, but are prone to extend rapidly over the surface. The disease is due to the introduction of a well-known micro-organism into the injured skin or mucous membrane, and it usually ceases spontaneously, after a definite duration, without leaving any changes in the affected tissues, although in rare cases more serious diseases of the skin or internal organs may follow.

Many explanations of the word erysipelas have been given. Although the most popular derivation, from ἐρυθρός, "red," and πέλλα, "skin," is very unlikely, we must also doubt that of Fehleisen, who traces the word to ἐρυθρός, "red," and πέλος = πελιός = πελλός, "blackish-blue" or "suffused with blood." The explanation of Villaret ("Handwörterbuch der ges. Med.," 1888, S. 450), who suggested the derivation from ἐρύω, "I move," and πέλας, "near," seems in any case equally correct. Erysipelas would consequently be a disease which extends to the neighboring tissues.

THE HISTORY OF ERYSIPELAS.

THE clinical picture of erysipelas, as we see it to-day, was known to antiquity. Hippocrates, Galen, and the later Greek, Roman, and Arabian physicians, as well as the medical writers of the middle ages, describe the course of the disease as it is seen in modern times. The older authors, however, were disposed to confuse it with a number of morbid processes which undoubtedly have nothing to do with the disease in question. Purulent and gangrenous affections of the skin and many diseases of the uterus and of the lungs were consequently described as erysipelas. Hippocrates even differentiated between idio-

pathic and traumatic erysipelas, and Galen between erysipelas and phlegmon. In addition to small, often unimportant injuries of the surface, they both considered the influence of the weather of etiologic importance. Galen, moreover, regarded the bilious change of the blood as the chief cause of the disease. This theory was dominant until near the middle of the nineteenth century. Even Rust[1] was convinced that erysipelas had certain relations with the biliary secretion, and so explained the value of purgatives in this affection. He separated erysipelas from phlegmon even more sharply than did Galen, since he designated all deep-seated processes progressing with suppuration as pseudo-erysipelas and eliminated many skin diseases, especially the acute exanthemata, which had previously been classified as erysipelas.

The views of the origin of the disease were equally confusing in the following decade, although Henle,[2] in 1840, by brilliant theoretic reasoning, made the lowest vegetable organisms the probable cause of the contagious diseases. In Germany they still clung to the theory of a bilious dyscrasia, when Wernher,[3] in Germany, and Velpeau and Trousseau,[4] in France, taught more or less definitely the contagiousness of erysipelas and emphasized its uniform dependence upon external injuries. With a characteristic and fiery eloquence the French clinician championed the proposition "that in almost every case of erysipelas a trivial injury of the skin may be found from which the so-called medical erysipelas has proceeded; that, however, the development of the process required an exciting cause, which plays the principal and not the subordinate rôle in the origin of the disease."

Volkmann,[5] in 1869, expressed himself in a similar manner, regarding erysipelas as a "local disturbance dependent upon the influences of a special poison." Hüter[6] soon followed with the more definite declaration that the infectious material was an organism belonging to the class of cleft fungi, and Lukomsky,[7] Billroth and Ehrlich,[8] as well as Tillmanns,[9] seemed to be upon its track. Fehleisen[10] was the first to succeed in proving, by careful investigations based upon Koch's postulates, that the exciting cause of erysipelas was, without exception, a streptococcus, which he designated as the Streptococcus erysipelatis. He differentiated between erysipelas and phlegmon still more sharply than the last-named authors, and was able to prove the correctness of his views by the bacteriologic examination of pieces of tissue taken from patients suffering with the disease. In opposition to Lukomsky and others, he found his micrococci only in the lymph channels and spaces, and never in the blood-vessels of the skin.

THE EPIDEMIC APPEARANCE OF ERYSIPELAS IN HOSPITALS, DWELLINGS, LOCALITIES, AND COUNTRIES.

Until near the middle of the nineteenth century, every medical writer pictured the epidemic appearance of erysipelas in addition to its sporadic occurrence, the description of hospital epidemics being particularly in evidence. Even Hippocrates knew that erysipelas showed a decided preference for wounds, and that it often proceeded from small and insignificant solutions of continuity of the skin. He explicitly emphasized the fact that not only neglected wounds, but also those carefully treated, might become the starting-point of the malady. Later on, however, there was a constant claim that the occurrence of erysipelas was to be attributed chiefly to deficient medical treatment of wounds. Many hospitals were in bad repute on account of their frequent epidemics, and this was not without reason, for it was definitely known that every case operated upon became erysipelatous in certain wards, and that many of them succumbed. Boinet described such a condition of affairs at the Hôtel Dieu in Paris; so did Wells in various London hospitals at the end of the eighteenth and beginning of the nineteenth century. Hospital epidemics were described at the Hôtel Dieu in Montpellier by Serre in 1840, at the Zürich Krankenhaus by Billroth and Waeckerling in 1859–1860, at the surgical clinic in Heidelberg by Ponfick in 1866, at the Hôtel Dieu in Lyon by Ollier in 1867, and at the surgical clinic in Halle by Volkmann in 1868 (see Hirsch[11]).

The uniform and often repeated appearance of erysipelas in certain hospitals and in individual wards gave rise to the suspicion that the virus of the disease clung to a locality, and that its development and dissemination were furthered by certain hygienic errors. Frequent observation has taught that ward epidemics always start from a definite case. Thomson[12] records the following experience from the Middlesex Hospital in London:

In a roomy ward, situated upon the ground floor of the hospital, erysipelas repeatedly appeared in two beds, situated one upon each side of a window. Upon examination an uncovered sewage ditch was found immediately beneath this window, and its vapors thus gained access to these particular beds. After carefully covering over the ditch the endemic completely ceased. Some time later, when the disease broke out again in these beds, it was found that the ditch was again uncovered. Care was taken to close it permanently, and the disease disappeared for ever.

A similar observation comes from Busch[13], who had a bed in a beautiful airy ward in his clinic at Bonn, in which an operation case

could not be placed without exposing it to the danger of infection with erysipelas. In this instance an imperfect drain allowed effluvia to escape, which led to the disease in the hospital.

Mention must also be made of the experience of König, who observed a small endemic of erysipelas in the surgical clinic at Rostock. The cause was, without doubt, a soiled and blood-soaked cushion upon the operating table. The erysipelas ceased immediately upon the removal of this cushion, whereas previously every one who had lain upon the fatal object had been infected.

On the other hand, distinguished investigators, surgeons especially, had contradicted the statement that hospital endemics were caused merely by overcrowding and other hygienic errors. They pointed out that erysipelas appeared in modern well-ventilated hospitals which were not overcrowded, and that it could be due only to a specific exciting cause. Volkmann saw the disease continue in his clinic in spite of the most scrupulous cleanliness, Fergusson made the same observation in the best hospitals of London, and Ollier could, until 1867, carry out the most severe operations without fear of erysipelas, while after that date the majority of the cases operated upon were attacked (Hirsch).

Erysipelas epidemics were observed also in educational institutions, in hospital ships and other vessels, and in the docks of Devonport and Portsmouth.

The disease repeatedly showed itself, in different cities, as a spreading epidemic independent of the more poorly ventilated factories and workhouses. Such epidemics were seen in Boston (1832), in Bonn (1849), in Edinburgh (1850), in Kreise Pless in Silesia (1856), in North Greenland (1861), in Bordeaux and Paris (1863), and in Oxford (1874) (Hirsch).

While the erysipelas in the above-mentioned epidemics presented the same clinical picture as it did in sporadic cases, it showed a thoroughly malignant typhoid character in the frightful epidemics that visited America in the years 1822–36 and in the beginning pandemic of 1841. Hirsch collected from the "best sources" reports of no less than 70 epidemics that were observed in America at the time mentioned.

In addition to the erysipelas of the face and head, which very frequently also involved the remaining portions of the body, the patients suffered from severe disturbances in the pharynx and upper air-passages, putrid suppurations, gangrenous processes in the subcutaneous areolar tissue, and the gravest constitutional symptoms. We will subsequently return to this form of erysipelas, but wish to mention

Volkmann's opinion of this American pandemic.   He did not consider the disease to be erysipelas, but looked upon it as an affection closely related to diphtheria—probably even a pure pharyngeal diphtheria.

GEOGRAPHIC DISTRIBUTION OF ERYSIPELAS.

According to Hirsch, erysipelas exists in all parts of the globe.   It is rarer in the lower than in the higher latitudes, and is equally prevalent in the temperate zones of the eastern and western hemispheres. In the tropics and in Japan, it is said rarely to occur, but reports from these sources are generally unreliable.

INFLUENCE OF CLIMATE, SEASON, AND SOIL.

Although the geographic distribution of the disease teaches us that climatic influences have no decided causal significance, the fact must, however, be emphasized that the disease occurs more frequently during the cold seasons than during the warmer ones.   Cold, damp weather undoubtedly favors the appearance of erysipelas, or, what is more likely, it makes the individual much more susceptible to the disease germ.   The belief in the influence of the weather, which has held sway since Hippocrates, has been confirmed to this extent by careful series of observations based upon experiences of from ten to fifteen years (Frickhinger[14]).   It is nevertheless generally acknowledged that sporadic erysipelas has not infrequently occurred during the hot and dry summer months.

From time to time an explanation of an increase in erysipelas has been sought in a continued high level of the ground water.   Thus, Boinet states as an actual fact that with every high tide in the Seine an increase of the disease was noted in the wards of the Hôtel Dieu which were situated upon the river bank.   On the other hand, experience has taught that other hospitals situated in equally damp positions have remained free from erysipelas in spite of these apparently unfavorable conditions.   Last, but not least, the antiseptic treatment of wounds proved that even in the dampest hospitals erysipelas, as well as other wound infections, could be decreased or even extinguished (see Prophylaxis).   This fact stimulated exact investigation, and supported, more than any of the above-mentioned observations, the opinion that erysipelas was caused by a low organism.   We have already stated that these investigations were crowned with success.   It is now fitting that we should follow the steps which led to the discovery of the specific cause of the disease and give a description of its peculiarities.

ETIOLOGY.

Historic Review of the Etiologic Investigations.—Examples of the Transmission of Erysipelas from Patient to Patient and of Transmission by Instruments.—The Relations between Puerperal Fever and Erysipelas, and between Scarlatina and Erysipelas.—The Deciding Bacteriologic Investigations Concerning the Cause of the Disease.—The Identity of the Streptococcus erysipelatis and the Streptococcus pyogenes.

HISTORIC REVIEW OF THE ETIOLOGIC INVESTIGATION.

Every case of true erysipelas is caused by the introduction of streptococci. With a few insignificant exceptions, which will be considered later, the micrococcus gains access to the lymph paths through solutions of continuity of the skin or mucous membranes, whether they be minute fissures, abrasions, or wounds due to accident or operation. Although the wound infection in such instances is at once apparent, there remains a considerable group of cases in which the point of entrance is by no means clear. It was this fact which, for centuries, furnished the favorite differentiation between idiopathic or medical (cryptogenetic) erysipelas and the traumatic variety. According to modern ideas, this division has simply a historic value, and, though occasionally adhered to, it is simply from a practical standpoint, since the prognosis between the so-called idiopathic erysipelas and traumatic erysipelas is appreciably different. The proposition that erysipelas, in all of its phases and under all conditions, is due alone to the streptococcus is indisputable.

The following data prove the truth of this statement:

1. EXAMPLES OF TRANSMISSION FROM PATIENT TO PATIENT.

Reliable observations had taught that an immediate transmission of erysipelas from patient to patient could occur in previously immune lodgings as well as in hospitals. This may be illustrated by a series of examples:

Martin[15] (in Zuelzer's article on "Erysipelas" in the English edition of von Ziemssen's *Cyclopædia of the Practice of Medicine*, 1875, vol. II, p. 434) saw a fatal erysipelas following upon an abortion in a young woman. A few days later the husband, and a woman who had nursed the patient, contracted the disease.

Trousseau* treated a woman who had contracted a severe facial erysip-

*Clinique médicale de l'Hotel Dieu de Paris, 1865. Paris: J. B. Baillière et Fils, Tome premier, page 171.

elas nursing her husband, who had a gangrenous erysipelas of the prepuce following upon a urethrotomy. [Trousseau's description is given on page 433.] The day before his death the wife had chills, a day later sore throat, and in the next twenty-four hours a typical facial erysipelas, which resulted in her death. The chambermaid who had assisted in the care of the husband became sick at the same time as the wife, having sore throat and subsequent facial erysipelas.

Another observation of Trousseau's is equally worthy of note. A lady nursed her child for six months and then acquired a mammary abscess, which was opened by Nélaton. Erysipelas appeared in the wound several days later and spread over the entire opposite breast. The husband, an American marine officer, came to Paris, and two days later was attacked with an erysipelas that threatened his life. The disease started in an insignificant scratch that he had acquired during the railroad journey.

Lühe (according to Zuelzer) treated a boy for an erysipelas that had proceeded from a punctured wound of the arm. Six days later his brother, who slept with him, developed a bullous erysipelas of the face and scalp. Two days subsequently the sister who nursed them both was similarly attacked. No other case appeared in the city or its neighborhood.

Pujos (according to Zuelzer) saw a fatal gangrenous erysipelas develop in the injured leg of a hunter. His brother, who nursed him, was attacked with a similarly fatal erysipelas of the face and scalp. The disease was further transmitted to a daughter, to a nurse, and to a washerwoman who handled the patient's linen.

Another observation of Zuelzer's may be added. A woman acquired for the eleventh time an extensive erysipelas that always proceeded from a chronic coryza. The patient's two daughters, a neighbor who repeatedly visited her, and the neighbor's scrofulous child were attacked, shortly after each other, with an erysipelas that in two cases similarly involved the face, scalp, and half of the back.

These examples, which have been culled from a large series of individual observations, certainly teach that the immediate transmission of erysipelas may take place from one individual to another, and that it may occur in previously immune localities and in the absence of an epidemic.

[The doctrine of the contagiousness of erysipelas, first promulgated by Wells* at the close of the eighteenth century, has been adopted in Great Britain and Ireland since the time of Graves, of Dublin (1826–1854). The editor submits the following evidence on this point from his own experience† :

"In November, 1874, I was placed by Dr. Stokes and Dr. Alfred Hudson in charge of a gentleman, aged thirty-seven, who was the sub-

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Transactions of the Society for the Improvement of Medical and Chirurgical Knowledge, 1800, vol. II, p. 213.

†*Eruptive and Continued Fevers*, 1892. Dublin: Fannin & Co. Page 206 *et seq.*

ject of progressive locomotor ataxia, and who, two days after exposure to cold, on Friday the 20th, displayed constitutional symptoms, which proved to be connected with an erysipelas of the scrotum. This first showed itself on Wednesday the 25th, and by the 28th it had become gangrenous and involved the penis. On the 30th the right groin was implicated, and next day an erysipelatous patch appeared on the back of the right hand. Toward midnight of this day, December 1st, a band of erysipelas spread across the nose and downward into the mouth, finally invading the tongue, which became hugely edematous. The urine was now considerably albuminous, specific gravity 1018. It deposited amorphous urates and a few fragments of granular tube-casts. The patient, after violent delirium, began to sink rapidly, and expired at 4 A. M. of Thursday, December 3d.

" A married sister, aged thirty-six, attended the patient with singular devotion for several hours before his death. On Tuesday, December 8th, she complained of sore throat and weakness. Her pulse was extremely rapid, and she looked seriously ill. Next day the throat felt and appeared to be better; but the mucous membrane of the nose looked unhealthy, and the orifice of the nostrils was swollen, puffy, and sore. On the following day the nasal mischief was more pronounced, but the throat continued to improve. On Friday the upper lip became edematous, and an attack of facial erysipelas was clearly in progress. On Saturday the swelling spread upward, and engaged the eyelids and forehead; across the latter a well-marked line of demarcation ran. Temperature in axilla was now 102.3°; pulse, 128. By 10 P. M. the inflammatory edema had engaged the left ear, and reached the hairy scalp. Temperature, 103.5°. On the sixth day the case was a typical one of facial erysipelas—pulse, 128; temperature, 103.8°.

" This lady's illness proved exceptionally severe, and for many days her life hung in the balance. The temperature rose to 105.4° on the evening of the tenth day, and violent delirium was followed by symptoms of profound nervous prostration and by paralysis of the bladder. Ultimately, she recovered perfectly. On January 11, 1875, I took this note: 'She is desquamating everywhere, as if after an attack of scarlatina.'

" It should be mentioned that the valet of the unfortunate gentleman, whose illness cost him his own life and placed his sister's in such jeopardy, was admitted to the City of Dublin Hospital on December 11, 1874, a few days after his master's death, suffering from abscess in the right tonsil and an unhealthy-looking herpetic eruption, involving the right side of the neck and the adjoining ear.

"On February 21, 1884, Jane M. was admitted into Cork Street Fever Hospital, Dublin, on the fourteenth day of a severe attack of facial erysipelas. She died next day. On February 25th, ward-maid Mary Lennon, who attended this patient, complained of not being well. On the 28th she was unable to leave her bed, complaining of severe shivering, headache, and pain in the back. It was ascertained that she was suffering from facial erysipelas. Incubation in this case was apparently four or five days.

"The most remarkable series of cases due to infection which have ever come under my notice occurred in the year 1882. They illustrate especially the intimate relation which exists between erysipelas of the throat and ordinary cutaneous erysipelas. In the month of February in the year named the secretary of the Meath Hospital occupied as his sleeping apartment one of the Collis Wards; in the other, separated by a central corridor, lay a surgical patient suffering from traumatic erysipelas. In a few days the secretary complained of painful sore throat, which was accompanied by severe constitutional disturbance, high fever, and extreme prostration. After a short time the larynx became engaged, and symptoms of edema of the glottis supervened. The treatment adopted happily proved successful, and the patient gradually recovered. He was devotedly attended and nursed by a sister who, in a few days, fell ill of a sharp attack of *facial* erysipelas, which ran a normal course. And now comes the interesting part of the story. During his sister's illness the secretary sent bulletins as to her state to a married sister living in the County Sligo, at a distance of 130 miles. Letters written by himself were despatched on the 10th and 13th of March, and a postcard followed on the 17th. The lady incautiously placed these letters and postcard under her pillow at night, with the result that on the 21st of March she sickened with severe sore-throat accompanied by intense pain and much swelling. She was attended by a domestic servant, who in a few days developed an attack of facial erysipelas."

Hirsch points out that epidemics complicated with throat affection have been repeatedly described. Of one such outbreak at Montrose in 1822, Gibson* says: "The disease was not so much confined to the head or face as common erysipelas, but it frequently attacked other parts of the surface of the body. *Sometimes the internal fauces were attacked*, and if it spread to the trachea it generally proved fatal."

Trousseau† narrates a strikingly similar instance to those I have

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*Trans. of the Edinburgh Med. Chir. Soc., 1828, vol. III, p. 94.
†*Clinique Médicale de 'l Hôtel Dieu de Paris*, 1865, vol. I, p. 171

just detailed of the spread of erysipelas and of its alternating phases in different individuals. I give his very words: "J'étais appelé en consultation par mon honorable ami M. le docteur Paris, auprès d'un M. E. . . . chez lequel un de nos chirurgiens les plus habiles, M. le Professor Nélaton, avait été obligé de pratiquer le débridement du méat urinaire afin de faciliter l'introduction d'instruments lithotripteurs. M. E. . . . succombait à un érysipéle gangréneux du prépuce, qui avait eu pour point de départ cette petite incision. La veille de sa mort, sa femme, qui l'avait soigné avec une grande sollisitude, fut prise de frissons; le lendemain elle avait une angine violente, et vingt-quatre heures après un érysipèle de la face d'une extrême gravité, qui l'emporta alors qu' elle semblait entrer en convalescence. La femme de chambre tomba malade en même temps que sa maîtresse, elle n'avait cessé de donner des soins à M. E. . . . La maladie chez elle fut caractérisée surtout par une violente angine, et par un érysipèle qui se limita aux paupières."]

Endemic Occurrence in Hospitals.—The painful observation has repeatedly been made that erysipelas may be introduced into hospitals from without and give rise to an endemic. Antisepsis has fortunately taught us how to meet this danger better than we could have met it in former days, and we are forced to furnish illustrative cases from pre-Listerian experience.

Bernutz (in Zuelzer's article) records the following: In November, 1864, a patient with facial eczema was discharged from the Hôpital St. Louis because erysipelas had broken out there. Four days later she had facial erysipelas, and was admitted to the Hôpital de la Pitié, where no erysipelas had been observed up to that time. On the next day the women in the two adjoining beds and a third patient were attacked by the disease.

Cornil saw, some days after the admittance of an erysipelas case to the Hôpital Beaujon, a typhoid convalescent, a smallpox convalescent, and a patient with pericarditis stricken with erysipelas, although it had not previously occurred in the hospital.

Labbé transferred an erysipelatous patient from the surgical wards of the Charité, where an erysipelas epidemic existed, to the medical wards, which had up to that time escaped the disease. The patient died, her nearest neighbor contracted the malady, and the erysipelas spread throughout the medical department.

Martin's case in the Hôpital de la Pitié was that of a man who was attacked by erysipelas, after a sequestrotomy, and soon succumbed. Three days later there were three cases in one ward and two in another, although no erysipelas had been previously observed.

The natural suspicion that in such hospital cases the disease is further spread by physicians or nurses is not to be summarily dismissed. We must, however, emphasize the fact that transferred or

recently admitted cases have introduced the disease-producing material into previously immune wards, in which physicians and nurses have been actively engaged. In the second place, the way in which the disease spreads in individual wards points to its immediate transmission through the air or from one patient to another.

The following experience of Goodfellow (Hirsch[11]) supports this view:

In an epidemic of typhoid fever at the Fever Hospital (autumn of 1833) erysipelas was continually present in the wards, and as a rule the disease spread from bed to bed. This was particularly noticeable in one ward containing 13 beds, 7 upon one side and 6 upon the other. The patient in bed No. 2 developed erysipelas; shortly afterward the patients in beds No. 1 and No. 3 were attacked simultaneously, after that the patient in bed No. 4 was affected, and finally the disease advanced regularly along one side of the ward. On reaching the last bed it sprang across the ward and again continued its regular progress. The patient in bed No. 13 was the only one who did not contract the disease.

2. TRANSMISSION BY INSTRUMENTS.

There are reliable observations, especially among those made in earlier times, which show the direct transmission of the disease germ by means of infected instruments and dressings. The sad experiences of many vaccine physicians and the intentional transmissions of the disease for curative purposes are particularly instructive. Since this subject will be thoroughly treated further on, we will simply mention that Doepp[16] saw the disease develop in 9 children who had been vaccinated with lymph obtained from a case of vaccine erysipelas.

3. THE RELATIONS BETWEEN PUERPERAL FEVER AND ERYSIPELAS.

The simultaneous appearance of puerperal fever and erysipelas has always seemed worthy of note. Distinguished physicians have not only suspected, but more or less positively declared, that there is a certain causal relation between the diseases.

At the end of the eighteenth century especially, the English physicians in the lying-in hospitals of London were impressed with the frequent coincidence of the two diseases. Similar observations accumulated during the erysipelas pandemic in America, and were obtained at a later date from German and Austrian institutions.

In addition to many other individual experiences which will be considered later, the following observation of Pihan-Dufeillay is very instructive: In the early months of the year 1861, the Hôpital St. Louis was visited by such a malignant and rapidly spreading epidemic of

puerperal fever that new cases were refused admittance and the puerperal women and other patients were transferred to other wards. The vacated places were filled by 32 women affected with chronic skin diseases, and many of them soon contracted erysipelas. Some of these cases were very severe, and one ended in death (Hirsch[11]).

Furthermore, it had frequently been established that fatal puerperal fever was ushered in by an erysipelas of the external genitals, and that the children of women who were not affected with erysipelas, but who had puerperal fever, were frequently attacked by true erysipelas and usually perished.

Lastly, experience had frequently taught that physicians, midwives, and nurses coming in professional contact with erysipelas cases could transmit puerperal fever to freshly delivered women, and, vice versâ, that they could themselves contract erysipelas if they had to do with cases of puerperal fever.

The following examples may be mentioned:

1. Spencer Wells[17]: A physician suffering with a mild erysipelas of the forearm attended two confinement cases in which the labor was normal and only required his presence for a short time. Twenty-four hours later both patients had puerperal fever, which terminated fatally within five days.

The same physician observed a case of child-bed fever which ended fatally in thirty hours. The patient's nurse had developed facial erysipelas a few days before the delivery.

2. Krauss,[18] in 1872, saw an epidemic of puerperal fever that was surely traced to the local midwife. This individual was recovering from an attack of facial erysipelas, and while still desquamating delivered a woman on October 2, 1872. The patient was attacked by puerperal peritonitis on October 4th, and died upon the following day. During October and the beginning of November the midwife attended 9 other women. All of them had fever and the majority (7) died. At the same time there was a small epidemic of erysipelas in Reichenbach and its neighborhood. In Reichenbach itself there were 8 cases, 2 of which terminated fatally.

3. Wegscheider[19] records an equally tragic result of the work of a Berlin midwife. In one day (October, 1868) she delivered 4 women, who all died from a rapidly progressing puerperal fever. On the day in question, the midwife had a beginning facial erysipelas, and subsequently became so ill that she was confined to bed for two weeks and was unable to follow her occupation until a week later. Contrary to medical advise, she neglected the cleansing of her clothes and instruments and engaged in active work. The result was that of the 22 women attended by her from October 21st until November 4th, 9 were attacked by puerperal fever and 6 died. The 13 who escaped were multiparæ who had received scarcely any attention from the midwife.

4. Lee saw a physician and nurse, in attendance upon a case of puerperal fever, develop erysipelas simultaneously. The baby also contracted the disease (Hirsch).

5. Squire relates the following chain of circumstances (Hirsch): He visited a man suffering with traumatic erysipelas, and immediately afterward delivered a woman who died on the sixth day. The man died two days later. Soon afterward a second woman, who had come from the house of the erysipelas patient, was stricken with a fatal puerperal fever. There quickly followed 8 new cases of erysipelas, 3 of which were fatal, in people who had been known to visit the puerperal woman and who had suffered from slight injuries of the skin.

6. In the Reichenbach epidemic of puerperal fever, Krauss saw surgical erysipelas develop in 4 newly born children, whose mothers already had fever. Two of these cases were fatal.

In view of such experiences it is easy to comprehend that for years well-known physicians have not doubted the relationship between the exciting causes of erysipelas and puerperal fever, and that many, such as Nunnelly (London, 1849), even claim their complete identity. It will presently be shown that the newer bacteriologic investigations support this theory.

4. THE RELATION BETWEEN SCARLATINA AND ERYSIPELAS.

Whether or not relations exist between scarlet fever and erysipelas similar to those that have we just considered between puerperal fever and erysipelas, is by no means clear. The subject has always received serious consideration, and the experiences of many, to which we will add our own observations, suggest the existence of such relations. The question is still an open one, and the blunt denials with which it has been met by Baumgarten and von Jürgensen are not sufficiently supported.

This much is certain: Erysipelas is a contagious, directly transmissible disease that holds definite and peculiar reciprocal relations to puerperal fever. Transmission not only occurs from patient to patient, but can also take place through intermediate individuals, who carry the disease germ on their bodies, clothes, or instruments. This germ may also cling to certain localities, as is particularly proved by the above-cited hospital observations (Thomson,[12] Busch,[13]). These facts finally led to the supposition that the disease was caused by an infectious agent, which would probably be found in the group of lower vegetable organisms.

5. THE BACTERIOLOGIC INVESTIGATION OF THE CAUSE OF THE DISEASE.

As we have already briefly mentioned, Hüter[6] was the first who regarded a lower organism, in the group of so-called cleft fungi, as the exciting cause of the disease. Nevertheless, there can be no doubt that neither he nor the later investigators, excepting Koch[21] and Fehleisen,[10] had recognized or isolated the particular organism. All the above-mentioned investigators (see page 426) made the mistake of directing their histologic observations to cases which were not true uncomplicated erysipelas, and their investigations were, moreover, without conclusive value, since they attempted to solve the question without sufficient bacteriologic knowledge.

Almost simultaneously, Koch and Fehleisen followed out the method which alone promised success. Thanks to their investigations, and, above all, to the complete work of Fehleisen, it has been made absolutely clear that erysipelas is always produced by the streptococcus.

Fehleisen sharply differentiated between erysipelas and phlegmon, and confined his anatomic and bacteriologic studies wholly to true erysipelas. In the sections which he cut from pieces of skin obtained from erysipelatous patients and bodies he always found chains of micrococci in the lymphatic vessels of the skin and subcutaneous areolar tissues. The lymph tracts of the superficial layer of the corium were most densely packed. In opposition to Lukomsky, who had seen the small blood-vessels as well as the lymph tracts filled with cocci, Fehleisen emphasized the uniform immunity of the blood-vessels, and ascribed the findings of this and other authors to the fact that the cases were not true erysipelas, but erysipelas complicated with pyemia. In the two cases of pure erysipelas examined by Lukomsky the findings agreed exactly with his own.

The uniform occurrence of this same streptococcus indicated the probability of its specific pathogenesis. The final proof, however, was wanting until Fehleisen[22] made his rigidly methodic investigations, based upon the principles laid down by R. Koch.

Attempts to obtain pure cultures of the coccus from the contents of freshly opened erysipelas vesicles were devoid of result. Sometimes the specific cocci were absent; sometimes they were associated with other bacteria, which grew more rapidly and overcame them; in other instances they were already dead. Pure cultures were finally obtained by removing small pieces of the carefully cleansed skin of the patient with sterile scissors and placing them in melted gelatin. Tubes of this

gelatin were placed in an incubating oven for two hours and then poured out into Petri dishes. These cultures were kept at room-temperature. In two or three days small, white, punctiform colonies developed, which grew best upon the surface, and even then attained only the size of a pin-head. The streptococcus did not liquefy gelatin.

Upon agar at a temperature of 37° C. (98.6° F.) a fine, transparent, colorless growth was observed, within twenty-four hours, which consisted of closely set, though not actually confluent, colonies. The colonies upon agar, even when growing alone, likewise did not exceed the size of a pin-head. The microscopic appearance of the colonies was that of dull, yellowish-brown, finely granular, rounded heaps.

In bouillon the growth is characterized by a thread-like, flocculent, yellowish-white deposit, the supernatant fluid remaining clear.

These cultures have a very limited duration of life, usually dying within a few weeks. If they are cultivated for two days at a temperature of 22° C. (71.6° F.), and the gelatin cultures placed in an ice-chest, they will, however, retain their vitality and virulence for months (Petruschky).

In cover-glass preparations the streptococci form more or less wavy chains of varying length.

Pure cultures of the streptococci produced true erysipelas in the ear of the rabbit. In from thirty-six to forty-eight hours after the inoculation, Fehleisen observed an increase of temperature of 1° to 1.5° C. (1.8° to 2.7° F.) and the development of a sharply circumscribed redness, which rapidly extended along the veins to the base of the ear. By transmitted sunlight the vessels were distinctly dilated in comparison with those of the healthy ear. After two or three days the ear became paler, while the inflammation extended to the head and neck, but here the redness was not so sharply outlined. After from six to ten days the disease ceased and the rabbits (6) recovered. In one case, when the erysipelas had reached the middle of the ear three days after the inoculation, Fehleisen amputated the entire member with the thermocautery. In sections cut from this ear he found the lymph paths crowded with streptococci, just as he had seen them in sections of the skin of erysipelatous patients.

Erysipelas, however, permits of a still further investigation, and of one that is usually impossible in experimental pathology. It had been observed since the eighteenth century that individuals suffering with lupus or malignant disease were occasionally improved or completely cured by an attack of erysipelas. Fehleisen was in the position to carry out inoculation experiments with his pure culture in 7 individuals

who either had inoperable growths or lupus. The first six cases developed typical erysipelas, while the seventh, a young man of twenty, who had had lupus for twelve years and had passed through repeated attacks of erysipelas, was inoculated twice without developing the disease.

Clinical observation showed that the inoculated disease in the first six cases was undoubtedly true erysipelas. After an incubation of from fifteen to sixty-one hours, the disease commenced in all the patients with an initial chill and a rapidly appearing, sharply defined inflammation in the neighborhood of the point of inoculation. The redness spread to the surrounding tissues exactly as it did in ordinary erysipelas, and likewise advanced over areas of varying size, with a continuance of the fever, and frequently with grave disturbance of the general condition. The duration of the disease varied between five and fifteen days. In all cases convalescence occurred without suppuration.

In two cases the inoculations were without result, and they were repeated after the patients had recovered from the first attack of erysipelas. The inoculation was also repeated in the young man who had had erysipelas three months before and had remained unaffected by the primary inoculation.

From his thorough investigations, Fehleisen was certain that the streptococcus which he discovered was the specific exciting cause of erysipelas, and that it showed both morphologic and biologic differences from the Streptococcus pyogenes. He particularly re-emphasized the fact that the Streptococcus erysipelatis always developed primarily in the lymph paths, and frequently extended in an opposite direction to that of the lymphatic stream, while the Streptococcus pyogenes was to be found only in the lymphatic vessels situated centrally from the primary point of suppuration. He also considered the sharp distinction between erysipelas and phlegmon as necessary from an etiologic standpoint.

Do Differences Exist between the Streptococcus erysipelatis and the Streptococcus pyogenes?—Fehleisen's view was supported by the statements of Rosenbach,[23] that the individual cocci of the Streptococcus erysipelatis were larger than those of the Streptococcus pyogenes, that cultures of the former were of more rapid growth, and that the Streptococcus pyogenes grew more in the form of an acacia leaf, whereas the Streptococcus erysipelatis resembled more closely the leaf of the fern.

Hajek[24] considered all three characteristics as delusive, and

claimed that the two forms of cocci differed only in their manner of spreading through the body, since the Streptococcus erysipelatis extended exclusively through the lymphatic system and the Streptococcus pyogenes distinguished itself by its unlimited invasion of the tissues. The continued bacteriologic investigation of other authors, however, showed that such a difference could not be maintained.

In several instances von Eiselsberg[25] was successful in producing true erysipelas without infiltration, in the ears of rabbits, with a streptococcus culture obtained from a phlegmonous suppuration. The histologic appearance of these specimens corresponded exactly with the descriptions of Fehleisen. E. Fränkel,[26] employing a culture of the Streptococcus pyogenes from a peritonitis, produced typical erysipelas in the rabbit's ear, panophthalmia, abscesses under the skin of the back, and, in mice, a similar purulent peritonitis. The fact was not to be denied that the streptococcus of erysipelas as a rule produced erysipelas alone, while the Streptococcus pyogenes usually caused suppuration. The greatest advance should be credited to Widal,[27] who attributed this condition of affairs to varying degrees of virulence of the same streptococcus. After intravenous injection of rabbits with pure cultures of Streptococcus pyogenes the animals died, and pure cultures of the streptococci obtained from the heart's blood invariably produced nothing but erysipelas when introduced into the ears of other rabbits.

These experimental results supplemented the observations at the bedside in a most essential and valuable manner. Certain proof is furnished by various authors that the streptococcus of erysipelas can also produce suppuration in man.

In 1886, Hoffa[28] had already described a case of purulent inflammation of the knee-joint, that had appeared in the course of a true erysipelas ambulans. In the pus obtained by puncture, and later by direct incision, he obtained streptococci which not only showed a complete morphologic resemblance to those of Fehleisen, but which also produced an erysipelas which wandered over the head and neck of the inoculated rabbit. Von Eiselsberg detected identical streptococci in cutaneous abscesses, Simone[29] found them in internal abscesses and in the skin of a case of pyemia due to erysipelas, and von Noorden[30] and Widal recorded similar experiences. In an abscess of the lid following cutaneous erysipelas, the latter author found the selfsame coccus both in the skin and in the pus from the abscess; he likewise saw it in a phlegmonous abscess subsequent to an erysipelas of the leg. The latter case was of particular interest, since it infected five individuals,

two of whom died. In one of these cases an erysipelas of the head was followed by multiple small abscesses of the scalp, all of which contained the Streptococcus erysipelatis.

It was but natural that some bacteriologic proof should be sought concerning the relationship between puerperal fever and erysipelas. Upon the strength of personal observations Gusserow[31] declared that the two diseases were completely dissimilar, and supported his views by experiments upon animals, which did not become septic after the injection of erysipelas cultures either into the peritoneal cavity or into the abdominal wall. He had also observed that puerperal women could be attacked by erysipelas without becoming septic, and that they could have erysipelas in addition to sepsis. Winckel[32] alone argued in favor of the close relationship of the cocci, since he had produced typical erysipelas, in the rabbit's ear, by injecting cultures of streptococci, which he had obtained both from the blood and from the internal organs (internal puerperal erysipelas) of a case of puerperal sepsis with erysipelas of the external genitals.

Since the streptococcus is found as the sole exciting cause of puerperal fever in the overwhelming majority of cases,—and this I do not doubt from my rather extended experience,—and since it has been proved that the streptococcus of erysipelas is no specific coccus, but that streptococci of various origins can produce the disease, all doubts concerning the common etiology of puerperal fever and erysipelas may well be dismissed.

Proofs of the Identity of the Organisms.—Curiously enough, until recently the most important control observations were carried out exclusively upon the rabbit's ear. The positive results so obtained could never claim any decisive significance, since erysipelatous inflammations of the rabbit's ear may be caused by other bacteria, even if this is but seldom the case, and the relative virulence for man and rabbit may be very different.

It still remained to be proved that streptococci obtained from non-erysipelatous affections in *man*, were able to produce erysipelas when transmitted to another *man*.

Not long since (1896), this experiment was repeatedly carried out by Petruschky,[33] with a positive result.

He was at first unable to produce erysipelas, either with fresh cultures from a case of true erysipelas, or with streptococci increased in virulence by passage through animals. He finally inoculated two inoperable cases of carcinoma with a pure culture of streptococci from the fresh pus of peritonitis. The inoculation was carried out by means

of scarifications, as advised by R. Koch, and produced a typical erysipelas, which rapidly extended over the chest and back and was accompanied by high fever.

These positive results in man, which were in complete accord with the experiments upon animals already detailed by v. Eiselsberg, E. Fränkel, Widal, and Marbaix, furnished the final and conclusive proof that the Streptococcus erysipelatis could no longer be considered as the specific exciting cause of erysipelas. Typical erysipelas can be produced in the human individual also by streptococci which do not proceed from an erysipelatous patient.

The complete harmony of the clinical and laboratory results is shown by the following observations of Petruschky[34]:

1. A woman of twenty-one, admitted on account of an abortion, had an abscess under the breast. Erysipelas developed in the incisions, and long chains of streptococci were found in the phlegmonous suppuration. Before the various incisions healed, a new and more severe wandering erysipelas developed; cultures of streptococci obtained from the phlegmonous suppuration, as well as the pus itself, produced true erysipelas in the rabbit's ear.

2. A purulent mastitis opened spontaneously and led to an erysipelas that invaded a large area of the trunk and then attacked the breast a second time.

3. A woman of thirty had an erysipelas and a phlegmon at the same time; cultures of streptococci were obtained from her blood.

4. In another woman, who was attacked by a fatal erysipelas of the arm, Petruschky found the same streptococcus at the edge of the erysipelas and in the blood.

5. Two other women developed subcutaneous suppurations in the course of erysipelas; pure cultures of streptococci were found in all the abscesses.

We have here irrefutable proof that one and the same streptococcus can produce suppuration and secondary erysipelas, or vice versâ, and that the streptococcus may invade the blood. The latter fact, so frequently disputed in former times, was first established by Lebedeff,[35] who observed the intra-uterine infection of a fetus and demonstrated the Streptococcus erysipelatis in its lymphatic system. The streptococcus was also found in the blood-vessels of the lung in erysipelatous pneumonia (see cases of Denucé, Mosny, and Schönfield, page 470).

Later experiments by Petruschky,[36] under the direction of Robert Koch, in addition to many other interesting results, furnished the observation that a typical erysipelas could be produced eleven times in three and a half months, in a patient suffering with a tumor. The inoculations were made at intervals of one or two weeks, and then purposely discontinued. The case teaches that ten recoveries from as

many attacks of inoculated erysipelas conferred no immunity or increased power of resistance against streptococcus infections.

After all this we may accept as proved: That the streptococcus can not only produce erysipelas and dependent internal suppurations, but also the primary pus formation, whether or not it be followed by a true erysipelas; that a similar relation exists between puerperal fever and the coincident erysipelas; and, lastly, that general sepsis, which fortunately rarely follows or is accompanied by a true erysipelas, is due to the same streptococcus.

Although the conditions which influence the individual case are not clear, it is nevertheless to be assumed that the condition of the point of entrance, the individual local and general reaction and power of resistance of the individual, and the virulence of the streptococci, are all of decisive importance. The fact that the same streptococcus, which had previously caused only a harmless circumscribed erysipelas, is enabled by repeated cultivation to produce a grave general sepsis, gives us some understanding of the great variation in the results produced by this harmful parasite. It gives us a key to the previously enigmatic coincidence of epidemics of erysipelas and puerperal fever. We appreciate why, in such times, when the virulence of the germ was markedly increased by local and temporary conditions, the erysipelas assumed the malignant character described by Trousseau; we understand the outbreak of an erysipelas epidemic in the ward of the Hôpital St. Louis, from which septic puerperal women had just previously been removed; and the reciprocal relations of the two diseases as shown upon page 435 are also clear.

In our considerations so far we have assumed that the streptococcus was, without doubt, the only organism that could be considered as the cause of erysipelas. Although, in our opinion, no doubt of this can exist, we will not neglect to point out two cases of M. Jordans,[37] in which he could find only the Staphylococcccus pyogenes aureus. He considered himself justified in concluding that the particular form of the disease was not dependent upon the kind of bacteria present, but upon their localization.

1. A baker, sixteen years of age, was suddenly attacked by a redness and swelling of the nose, forehead, and cheeks, with a chill and other constitutional symptoms. After several days of continuous fever both eyeballs became prominent, the right leg swelled, a phlegmonous inflammation appeared upon the forehead, and a wandering pneumonia developed in both lower lobes. The temperature gradually sank to normal at the end of the third week. In a few days the erysipelas recurred, starting in the fistula upon the forehead. Recovery occurred after three months.

The Staphylococcus pyogenes aureus was found in the periosteal pus from the leg and from the forehead, in the fluid obtained by puncturing the pneumonic exudate, in excised pieces of the skin, and in the blood (previous to the recurrence upon the forehead).

2. A new nurse, who had tended the patient for three days, developed a chill, fever, vomiting, and a typical facial erysipelas. After three days the redness disappeared and the temperature fell by crisis. Recovery was complete in six days.

A fine puncture was made at the edge of the erysipelatous area, the exuded drop of clear serum was transferred to agar-agar, and a pure culture of the Staphylococcus pyogenes aureus was cultivated.

According to our judgment, these cases prove nothing in the face of many hundreds of observations to the contrary effect. The second case certainly demands consideration, inasmuch as it seems striking that sufficient material to produce a pure culture was obtained from the fine puncture. Errors occur too easily by this method, and it cannot be regarded as free from objections.

The Occurrence of the Streptococcus outside of the Human Body.—From the general distribution and occasional endemic and epidemic outbreaks of erysipelas, there is no doubt that the exciting cause may multiply outside of the human body. Many clinical experiences show that its virulence may be increased by temporary and local external conditions.

The experiences of Thomson and Busch (see page 427) permit the conclusion that the streptococci found a permanent culture-medium, in which they developed and increased in virulence and from which they repeatedly renewed their attacks. The more frequent occurrence of erysipelas in the cold damp months of spring and autumn indicates that the cocci are favored in their development by these particular conditions of the weather.

Exact experimental proof of the existence of virulent streptococci in the air of surgical wards was furnished by v. Eiselsberg,[38] who placed gelatin plates in the neighborhood of erysipelas cases and always obtained cultures of streptococci. If the plates were exposed in rooms containing no erysipelatous individuals, the streptococci were not demonstrable.

It is very probable that the infectious germs cling to instruments and clothing, and that they may be transmitted by them. The experiences of medical men recorded on pages 428 and 434 support this statement.

The simple presence of the germ, however, is as little able to produce infection as is the simultaneous presence of individuals with

trivial injuries. Both of these predisposing causes are almost daily furnished by hospital physicians and nurses, and yet they are proportionately rarely attacked by the disease. The uncommonly frequent recurrences of the disease show that an individual predisposition plays an important rôle. Disregarding sore throat and articular rheumatism, there is no other acute infectious disease that so frequently recurs as erysipelas. Sometimes the relapse occurs as early as eight or fourteen days after recovery from the first attack, but more commonly six or twelve months intervene before the relapse takes place. The supposition that the relapse is due to "retained slumbering" germs is not to be summarily dismissed, though it is difficult to prove. The undoubted cases of menstrual erysipelas might be cited in favor of such a theory. There are women who develop erysipelas, during the catamenial periods, in recurring cycles of from four to five weeks' duration. Hirtz and Widal[39] record the case of a woman who had 20 attacks of erysipelas during a three months' stay in the hospital. Four years before admission she had fallen into the water, and since that time she had not menstruated. The first attack appeared four weeks after the accident, and from that time on the unhappy woman had only remained free from the disease for two months. The same authors cited a second case, in which the erysipelas appeared at the menopause and relapsed at intervals corresponding to the previous menses. Since the observations come from earnest investigators, we have no right to doubt them, especially since the authors proved that the streptococcus was the exciting cause in the first case.

It also seems possible that hospital "habitués" are characterized by an especial susceptibility to this coccus, which favors its rapid increase, particularly during the spring and autumn, and facilitates the development of its specific pathogenic character. Chronic hospital cases, afflicted with prolonged suppurations, are frequently attacked by a recurrence within a few months. Outside of the hospital relapses occur mostly in individuals with chronic coryza and a tendency to the formation of fissures about the nostrils or on the lips. In such cases the point of entrance is clear. The frequency and course of relapses will be considered later.

It is not unlikely that the disposition to erysipelas is occasionally inherited. Roger[40] states that he has observed this so often that it cannot be ascribed to an accidental coincidence. This corresponds

with the experience of Schwalbe, who saw three generations of a family affected with habitual erysipelas (Zuelzer). Women are undoubtedly more disposed to the disease than men. In almost 700 cases from v. Ziemssen's clinic 26.91% were males, while 73.09% were females (Frickhinger[14]). Volkmann, Tillmanns, and others have also strongly emphasized the more frequent occurrence of erysipelas among women, and supported their statements by statistics from large series of cases.

PATHOLOGY.

1. THE PERIOD OF INCUBATION IN EXPERIMENTAL INOCULATION AND SPONTANEOUS OCCURRENCE.

IN the first experimental inoculations of pure cultures in the rabbit's ear, Fehleisen[22] saw the temperature rise 1.0° to 1.5° C. (1.8° to 2.7° F.) after thirty-six to forty-eight hours, and the simultaneous appearance of a sharply circumscribed redness at the point of inoculation. These observations, confirmed by numerous investigators, are of great importance, but the results obtained by the inoculation of cultures in man are more valuable and authoritative.

In Fehleisen's interesting series of observations we find that in one case the disease commenced fifteen hours after the inoculation, with a chill and a rise of temperature to 39.8° C. (103.6° F.); in the other cases the period of incubation lasted fifteen, twenty-three, thirty, and forty-seven hours respectively. While the chill was the first constitutional symptom in these five cases, one woman fifty-eight years of age, affected with multiple fibrosarcomata, developed a slight rise of temperature and chilliness seventeen hours after the inoculation. In the course of the day this was followed by loss of appetite, headache, and a further rise of temperature to 38.8° C. (101.8° F.). On the third day the general condition and temperature were normal. On the morning of the fourth day, sixty-one hours after the inoculation, there was a chill, a sudden rise of temperature to 40.5° C. (104.9° F.), and "a sharply circumscribed and slightly elevated redness as large as half the palm of the hand, a typical erysipelas marginatum."

Clinical observations are quite consistent with these figures obtained by experiment. In 41 cases of traumatic erysipelas Roger[40] found:

5 times	an incubation period of	7 to 18 hours
5 "	"	"	"	"	24 "
9 "	"	"	"	"	25 to 48 "
8 "	"	"	"	"	49 to 72 "

In the remaining cases the period between the injury and the commencement of the disease varied between four and twenty-two days.

Sometimes the redness of the skin is the first sign of the disease, though it commences with a chill at least as frequently. According to my personal experience and the descriptions of most of the text-

books, both symptoms are usually observed simultaneously. Trousseau[4] differs from this opinion. He admits that the fever sometimes precedes the dermatitis, but claims that this is rare, "and that the opposite condition usually obtains, since the dermatitis develops before the febrile reaction." In reference to this question, the following observations of Roger[40] are of interest:

At 10 A. M. a young man received a wound on the bridge of his nose from a fall upon the pavement. Seven hours later he felt a stinging in the wound, and noticed a redness and swelling, which was followed two hours later by a chill, vomiting, and fever. The next day he had an extensive facial erysipelas and a temperature of 39° C. (102.8° F.). Recovery was complete in twelve days.

Another gentleman injured his nose at 6 P. M. and awoke eight hours later with a chill. The erysipelas was not perceptible until five hours later.

The wife of a physician scratched herself at 9 P. M. by the introduction of an ear-ring which she seldom wore. At 4 A. M. she had a severe chill, and toward morning, her husband diagnosticated a typical erysipelas.

The question under discussion was disregarded by Fehleisen in his monograph. His first observation, however, showed a phenomenon that we occasionally see at the bedside—the appearance of slight prodromal erythemata, which might be mistaken for the first manifestations of the beginning erysipelas. In Fehleisen's Case I, as already mentioned, slight constitutional symptoms with a moderate elevation of temperature appeared upon the day after the inoculation. The points of inoculation showed a slight redness, but the chill did not occur until the fourth day, and four or five hours later an area of typical erysipelas as large as half the palm of the hand was seen. The same thing is seen in spontaneous erysipelas. A slight redness without swelling may appear on the alæ of the nose or at the canthus, without any other characteristic local or constitutional manifestation of erysipelas. The chill, the increased swelling, the sharply defined border, and the pain finally clear up the case. These cases may probably be due to the slight local irritation of moderately virulent streptococci, which, however, soon find more favorable conditions for their multiplication and nourishment, and are accordingly enabled to produce severe pathogenic effects.

In general, a prodromal stage is absent in erysipelas. The cases just described are to be considered as exceptions. We will subsequently refer to the preliminary sore throat and coryza.

In common with other authors, we believe that no relation exists between the length of the incubation period and the course of the dis-

ease.   Whether the erysipelas breaks out in seven to ten hours or in
six to eight days after the injury does not define the severity of the
disease.   Age, sex, and constitution are equally unimportant.   The
principal rôle is played by individual predisposition and the degree of
virulence of the streptococcus.

2. ONSET AND COURSE OF THE DISEASE.

It has been stated in the previous section that the disease is fre-
quently introduced by a severe chill and the simultaneous outbreak of
the exanthem, and that in a certain series of cases, sometimes the local,
sometimes the general symptoms are first observed.   No uniformity of
the mode of onset can be established.   Trousseau, it is true, states
that the cutaneous eruption very commonly precedes the febrile reac-
tion, but Roger saw the disease commence with severe constitutional
symptoms 310 times in 560 cases which he personally observed.   Every
hospital physician knows how uncertain the statements of patients are
in individual cases and how much may be obtained by leading ques-
tions.   The first trivial appearance of the cutaneous eruption is over-
looked, while the chill is so disagreeable that it is usually clearly re-
membered.   It consequently seems more correct for us to disregard
these fine differentiations, to a certain extent, and assume that the
disease is ushered in sometimes by the local, and sometimes by the
constitutional symptoms.   The situation and nature of the point of
entrance, the number and virulence of the bacteria, and the individual
predisposition have a defining influence in any given case.

(a) PHENOMENA IN THE SKIN AND IN THE LYMPHATIC GLANDS.
   —CHARACTER OF THE EXANTHEM AND ITS REGULAR EX-
   TENSION.—THE FORMATION OF VESICLES.—GANGRENE.

We will first consider the phenomena in the skin and lymphatic
glands.

In the great majority of cases erysipelas attacks the face.   In 140
cases, of which I possess individual drawings, the erysipelas remained
limited to the face; in 23 cases the face and scalp were attacked.

Among 597 cases, Roger saw involvement of the face alone 496
times; in 69 cases the face and scalp were affected.

The exanthem most frequently appears first in the immediate
neighborhood of the eyes.   The lids and their inner canthi, the cheeks,
and the bridge of the nose are the favorite sites of the commencing

eruption. The ears and their vicinity much more rarely furnish the starting-point of the erysipelas.

The eruption commences with one or more closely set, actively reddened, and somewhat elevated areas, which at first cause only an itching or a slight burning. With the usually rapid surface extension of the erysipelas, this sensation soon becomes one of disagreeable tension and increasing pain. The dermatitis is now marked; it is shown by the active and sharply defined redness, the increased heat, and the more or less tense swelling, which gives the skin a peculiar shining appearance. This dermatitis is clearly defined from the surrounding healthy skin by its sharply elevated border. Some portions of this border resemble segments of circles, while others show irregular projections of varying length which extend into the healthy skin. Numerous "outposts" are usually observed in the surrounding tissues, which seem to have separated from the main column and swarmed out to invade new areas.

[Billroth* uses a striking illustration when he says that the redness advances through the skin in many cases, just as fluids spread in blotting-paper, rounded tongue-like subcutaneous projections shooting out, which are followed by a broader advance.]

In spite of the apparently irregular method of extension of erysipelas, a certain regularity is unmistakable upon careful observation. This is explained by the structural relations of the skin, which Pfleger[41] has thoroughly elucidated, basing his observations upon the earlier anatomic investigations of Langer.[42] The latter author demonstrated that the skin is under different tensions in various portions of the body; that in some areas, almost no tension is present, while in other regions a uniform tension in all directions is observed. He showed that punctured openings made in the skin with a punch were quite regularly drawn in a definite direction, and that these "lines of tension" corresponded to the long diagonal of the rhombic meshes formed by the connective-tissue bundles.

The serum poured out in the skin and subcutaneous areolar tissue meets with least resistance in the direction of the lines of tension, and, consequently, in all areas in which the tension is not uniform we see the erysipelas advance with irregular and crested outrunners. If the tension is uniform with an indefinite line of fission, the disease extends quite diffusely.

Where the skin is denser and more firmly attached to the subjacent

*Lectures on Surgical Pathology and Therapeutics, New Syd. Soc., London, 1888, vol. II, p. 10.

tissues, the erysipelas finds a more or less distinct resistance.   At the base of the skull, at the crest of the ilium, at Poupart's ligament, and about the condyles of joints the erysipelas often stops and goes around the obstruction.   In such positions the so-called ligaments of the skin offer an actual check to the progress of the disease, and may arrest it completely if the exanthem is diminishing in intensity.   We now understand why the chin and upper portion of the neck are usually spared, and why the erysipelas is so often limited to the face and scalp.

The extension to the trunk does not take place over the chin, but, owing to these structural relations of the skin, it passes from the occiput to the neck and thence to the back.   The fact that an erysipelas originating in the breast almost never oversteps a horizontal plane between the thorax and abdomen is also due to the peculiar tension of the skin in this region.

If the erysipelas meets with an obstacle, the rapidity of extension is more or less retarded.   While the daily advances upon the cheeks, scalp, and back are often astonishing, in the above-mentioned situations the advancing border not rarely stops or is arrested after slowly passing several obstructions.   This dying out of the eruption is especially observed near the wrist-joint, when the fiery redness, advancing from the shoulder, goes slowly around the obstacles at the elbow, and then visibly pales in irregular projections upon the forearm.   The same thing may be observed in the gluteal region and in the lower extremities.

Whenever the erysipelas has gone around larger obstacles or remained stationary in front of them, small and larger isolated erysipelatous patches are occasionally seen which seem to have no actual organic relation with the main eruption.   It may be that the intervening neutral zone has a breadth of two fingers.

These cases have led to the false supposition that the eruption does not always spread by direct continuity of structure.   This view is surely fallacious.   The careful observer will always succeed in finding pale red streaks, composed of lymphatic vessels, which form delicate connecting bridges between the apparently separated erysipelatous areas.   Moreover, one must bear in mind that in rare cases the erysipelas may break out simultaneously in different portions of the body.   Volkmann, for example, saw erysipelas develop in both stumps of a double amputation.

The dermatitis presents a changing picture, which is determined partly by the severity of the inflammation and partly by the locality affected.   Where a uniform tension exists, the affected skin is usually

tense and shining, or the homogeneous infiltration may be felt (in the scalp, for example); in other parts, where the skin is more delicate and only loosely connected to the subjacent tissues, the inflammatory edema is marked. The latter condition is seen especially in the eyelids, which hang over the eyes like tense sacs and render impossible the opening of the palpebral fissure. The prepuce, scrotum, and labia also become misshapen and deformed. These localities are endangered, inasmuch as the skin may undergo necrosis if the excessive tension is of long duration. The same danger threatens those places which are situated immediately over the bones without the intervention of substantial cushions of fat, such as the skin over the zygoma, elbow, patella, tibia, and crest of the ilium.

When the skin is first involved, there is not only a spontaneous tension, but the parts are also sensibly painful to the touch. This teaches us that gentle palpation is of more value than inspection alone in outlining the erysipelatous area and its outrunners. As may be readily understood, palpation is of the greatest value in erysipelas of the scalp.

As a rule, the erysipelatous inflammation attains its greatest severity within two or three days. The redness and swelling then commence to disappear in the areas first attacked, while the inflammatory border advances, either as a whole or with irregular projections.

If the inflammation and tension are more marked, the epidermis is always elevated in the form of small, closely set vesicles, visible with a lens or the naked eye (*erysipelas miliare seu vesiculosum*), or in bullæ (*erysipelas bullosum*—"Blatterrose"). These vesicles contain either a clear serum or a yellowish-red fluid with numerous pus cells and microorganisms. The differentiation of the latter into pure cultures is rarely successful. The bullæ usually rupture spontaneously, quickly dry up, and, according to their contents, leave behind delicate lamellæ or thicker crusts (*erysipelas squamosum et crustosum*).

The adjacent lymphatic glands very frequently become swollen, palpable, and painful. According to Trousseau,[4] this inflammatory swelling should not only regularly occur, but "also nearly constantly precede the appearance of the erysipelatous eruption." From my own experience I cannot agree with this statement, though I must emphasize the almost regular occurrence of lymphadenitis, entirely agreeing with Küster,[43] who saw the swelling of the lymphatic glands appear "usually and very early." This author, however, adds that the lymphadenitis "not rarely occurs before the beginning of the dermatitis." Up to the present time I have met with no such case,

and I would explain the statement of Küster by the fact that his observations were chiefly upon surgical cases, in which lymphangitis and lymphadenitis may indeed be more frequent than in the erysipelas of the face and scalp with which physicians come into contact. It also seems worthy of note that the celebrated Parisian surgeon Velpeau[6] always considered the lymphadenitis to be a result of the erysipelatous dermatitis.

This much is certain—the lymphadenitis is one of the most uniform clinical phenomena of erysipelas, and deserves more careful attention than it usually receives from physicians.

As already stated, the dermatitis lasts only two or three days in the place first attacked, and then rapidly and completely disappears. As

Day of the Disease.
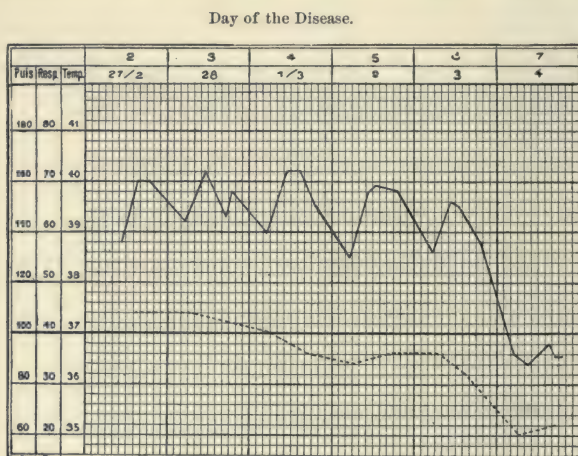
FIG. 13.

the inflammation decreases, the lymphatic glands usually also undergo a rapid resolution. Most cases of erysipelas tend to spread, and we see the daily advance of the sharply defined inflammatory border, while the area first involved becomes paler, decreases in size, and undergoes a more or less scaly desquamation. The rapidity of extension is variable. Sometimes the entire face becomes involved in a few hours, or "overnight," and again the area may be covered only by slight and repeated advances lasting several days (see figures on pages 457–459, which show the daily extension of the disease).

The duration of the erysipelas depends upon the extent of the disease. It usually amounts to eight or nine days if the face and scalp are alone involved; it may last several weeks or months if the disease assumes the type of a universal erysipelas migrans and wanders over

the entire body. In such cases the erysipelas may even pass over a previously involved area a second time. This variety of local recurrence is more commonly observed when the erysipelas involves the more extensive portions of the body than when the disease remains localized on the head. If the latter rare occurrence does take place, even an erysipelas limited to the face and scalp may last several weeks. In still rarer cases, the long duration of the disease may be due to its tardy extension.

Day of the Disease.
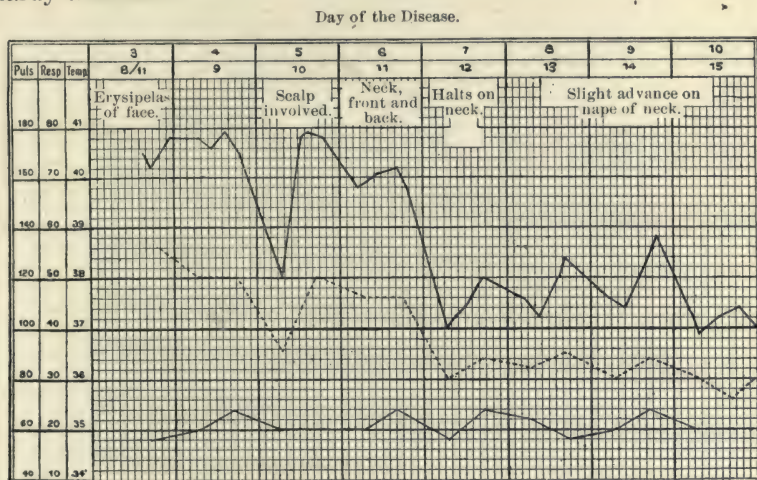
Fig. 14.

(b) THE COURSE OF THE FEVER IN ORDINARY ERYSIPELAS AND IN ERYSIPELAS MIGRANS.

In the majority of cases the outbreak of the erysipelas is introduced by a chill, vomiting, and a sudden rise of temperature to 40° to 40.5° or 41° C. (104° to 104.9° or 105.8° F.).

In many cases, especially those with active dermatitis, the body-temperature continues at this height for days, and then falls either by crisis or by lysis. Not rarely the temperature curve is less regular, showing a more marked morning fall on the second or third day, which is followed by a higher evening rise, so that the fever may assume a remittent or even an intermittent type. Although a rigid parallel between the grade of the dermatitis and the height of the fever is usually present, cases are occasionally observed in which severe constitutional symptoms and a violent inflammation are accompanied by a moderate temperature. Usually, however, the temperature curve corresponds so completely with the violence of the erysipelas that the

ERYSIPELAS.
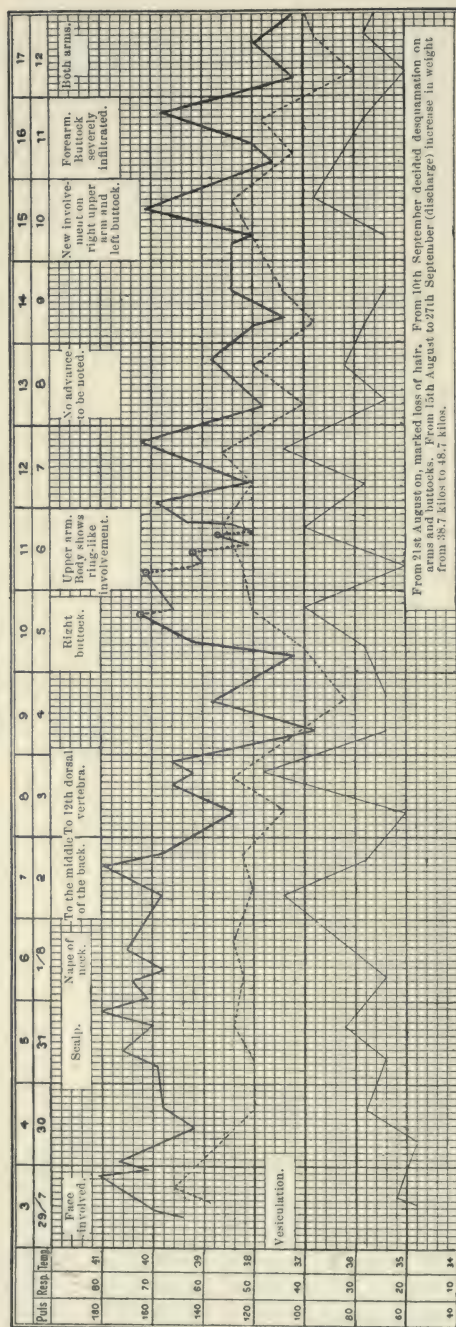
Fig. 15.

continuance or abatement of the disease may be predicted. A marked rise of the temperature indicates a rekindling of the inflammation.

The relapses,—recrudescences, "rechutte" of the French,—which begin after an afebrile period of one or more days, are also, as a rule, sooner indicated by a renewed elevation of temperature than by the
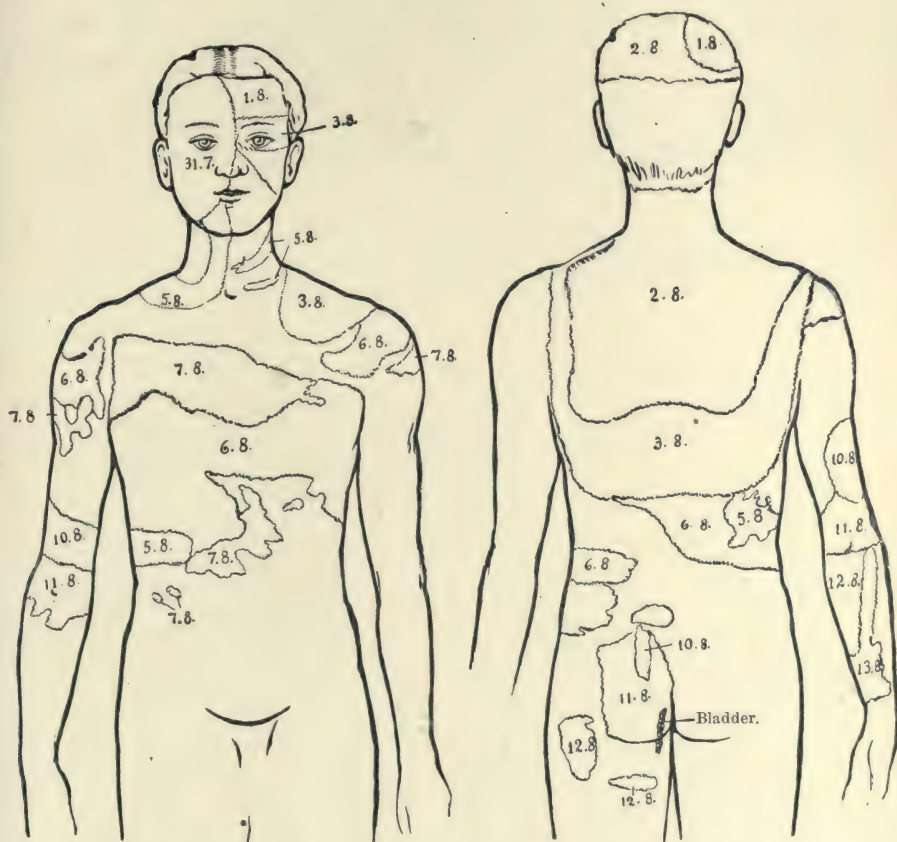
A case of erysipelas migrans with a graphic delineation of the daily advances.

FIG. 16.—Anterior view.   FIG. 17.—Posterior view.

local changes. Such relapses persist for several days, and may be repeated, especially in wandering erysipelas, as often as fresh outbursts occur. These renewed elevations of temperature usually become less marked as the disease declines, the last advances being indicated only by the evening temperature. A "critical perturbation" may precede the final fall to the normal.

In cases terminating unfavorably a high temperature is usually observed, which may continue to rise after death.

Contrary to the statements of many authors, I would say that, according to my experience, every erysipelas is accompanied by fever. The elevation may occasionally be slight or of very short duration, but it will never be missed if the temperature is carefully taken in the rectum every two or three hours. In my 140 cases, all of whom had fever, there were:

	With an average febrile period of
96 cases of facial erysipelas............................	7.9 days,
23 cases of erysipelas of the face and scalp.............	9.05 days,
17 cases of wandering erysipelas	18.08 days,
4 cases of erysipelas in an extremity	8.7 days.

This statement is in marked contradiction with the analysis of Roger,[40] who in 570 cases of erysipelas observed fever in but 315, and

FIG. 18.—Erysipelas migrans.   Anterior view.

in more than the half of these the febrile period lasted only three days. If the fever lasted more than a week, the case was a wandering erysipelas or had either recrudescences or suppurations. Roger himself seems to have been impressed with the small proportion of febrile cases, and he explains the marked deviation from the well-known state of affairs with the words "we do not include cases where transient fever may have existed before their admission under our care." This does not seem to be an acceptable explanation, and we are led to suppose that Roger's diagnosis of true erysipelas is not precise enough to correspond with our views.

Nevertheless I will not neglect to state that Frickhinger,[14] in the Munich General Hospital, saw 20% of all erysipelatous affections (including the relapses) pursue an afebrile course, and that Leube[44] "from personal experience can confirm the statement that, in rare cases, erysipelas may run its course without fever." From my experience, I would suspect that the apparent absence of fever in many

cases was to be attributed to the manner of taking the temperature. A case, presently to be mentioned, which came under my observation in the hospital was said to pursue an afebrile course, but measurements by the rectum, every three hours, demonstrated the existence of temperatures as high as 39.0° C. (102.2° F.). (See Fig. 22, page 461.)

Concerning the course of the body-temperature, and in addition to the charts contained in the section upon erysipelas of the mucous membranes, the following cases are instructive:

1. H., cabinet-maker æt. nineteen, was admitted on the second day of the disease. The erysipelas spread from the nose and in the following days involved the entire face as far as the roots of the hair and with the exception of the chin. Cessation of the disease on the sixteenth day (Fig. 13).

Figure 14 shows the course of the body-temperature in an erysipelas which was confined to the face until the fourth day. The temperature fell spontaneously on the fifth day and then rose rapidly as the disease spread to the scalp and neck. Complete cessation occurred upon the tenth day. Treatment exclusively with inunctions of vaselin. This was a first attack of erysipelas, and began with severe disturbances of deglutition.

· Figures 24, 25, and 26 also show the course of the fever in erysipelas of the face and scalp.

The next two charts, figures 15 and 20, represent the temperature curves of two cases of general wandering erysipelas. The advances on the anterior and posterior

Fig. 19.—Erysipelas migrans. Posterior view.

surfaces of the trunk are indicated upon the four sketches of the trunk.

In Clara S. (Fig. 15) there was an unusually rapid extension, since the erysipelas had already involved the entire back upon the eighth day of the disease. The irregular zig-zag temperature curve is well complemented by the sketches of the erythema (Figs. 16 and 17).

The course of the disease in K., æt. twenty-six, a shoemaker, on the contrary, seems to have been very quiet and regular. A strikingly uniform advance of the erysipelatous border occurred with a temperature continually varying between 40° and 41° C. (104° and 105.8° F.). So severe an involvement of the sensorium was present, however, that it was
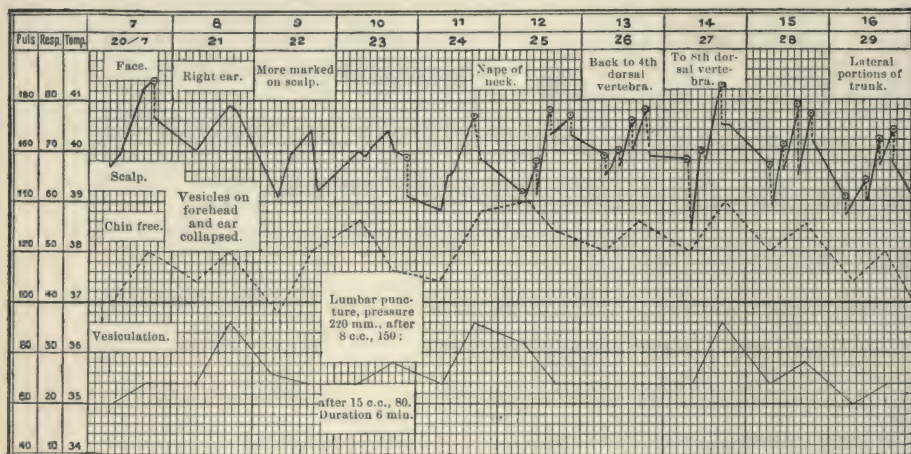
One year previously, facial erysipelas.

Fig. 20.
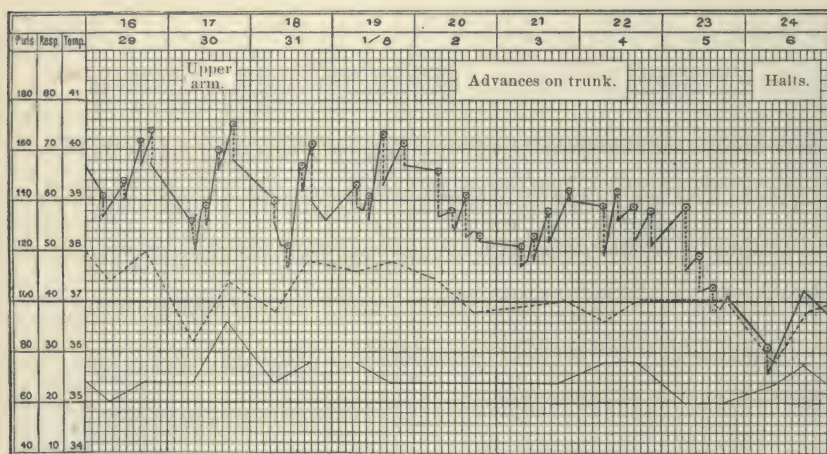
Fig. 21.—Continuation of the curve of figure 20.

days before the possibility of a meningitis could be excluded. Lumbar puncture revealed that not only the pressure, but also the amount of the cerebrospinal fluid was increased (Figs. 18, 19, 20, and 21).

Both cases resulted in complete recovery.

Figure 22 shows the course of a very mild erysipelas advancing

over the nose, right side of face, and right ear to the neck, in a typhoid convalescent. In the beginning it was regarded as an afebrile erysipelas until more frequent measurements by the rectum cleared up the condition of affairs (see page 459).

On September 20, 1897, boatswain S., æt. twenty, came under treatment for typhoid fever. In his convalescence he developed a paresis of the right serratus muscle. On the eighty-eighth day from the beginning of the disease the nose of the patient became swollen, actively reddened, and sensitive to pressure. During the next nine days the erysipelas gradually extended over the right cheek and ear. The general conditions were scarcely disturbed, the local annoyance was trifling, and the temperature was but slightly increased.

The etiology of this case was explained by the fact that a septic patient, in the next bed but one, had a few days previously developed erysipelas.
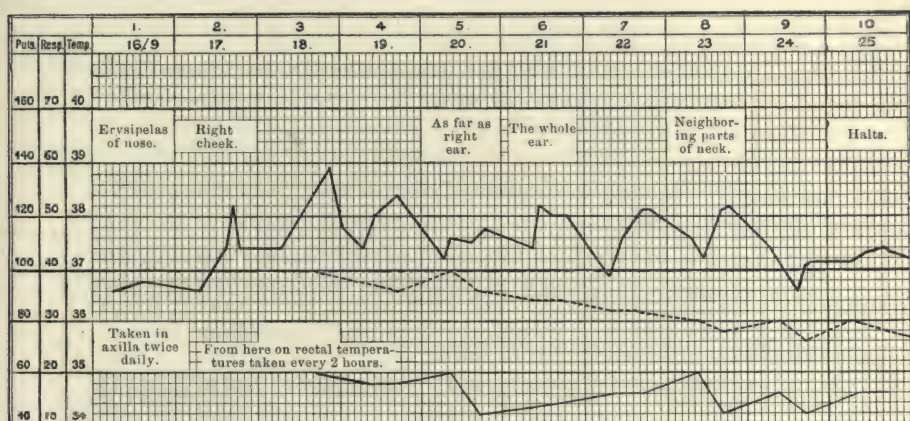
Fig. 22.

(c) ERYSIPELAS OF THE MUCOUS MEMBRANES.

Origin in the Throat; Extension through the Nose.—Cutaneous erysipelas is preceded by inflammatory phenomena in the mucous membranes more frequently than is commonly supposed. From a practical standpoint, it seems proper to first consider only the phenomena which are visible in the upper air-passages.

It is questionable whether every inflammation of the mucous membranes of the nose, throat, and larynx which precedes a facial erysipelas can be considered as the first manifestation of the disease, since a sore throat is also observed in the beginning of many other acute infectious diseases. But the frequency of its occurrence shortly before the appearance of a facial erysipelas, and the fact that the disease in these cases may not only develop in immediate continuation with the

inflammation of the mucous membranes of the nostril or lacrimal duct, but also extend in the opposite direction, from the face toward the mucous membranes, must remove any doubts which may chance to arise concerning this question.

Disregarding the primary erysipelas of the larynx, which offers certain characteristic signs, the erysipelatous sore throat and coryza are distinguished less by the local picture immediately presented than by their concomitant symptoms and sequelæ, especially by the secondary facial erysipelas.

Erysipelas of mucous membranes begins, as does cutaneous erysipelas, with local and constitutional symptoms, which either may occur simultaneously, or the one group may shortly precede the other. Sometimes, without any warning, a chill with marked febrile phe-
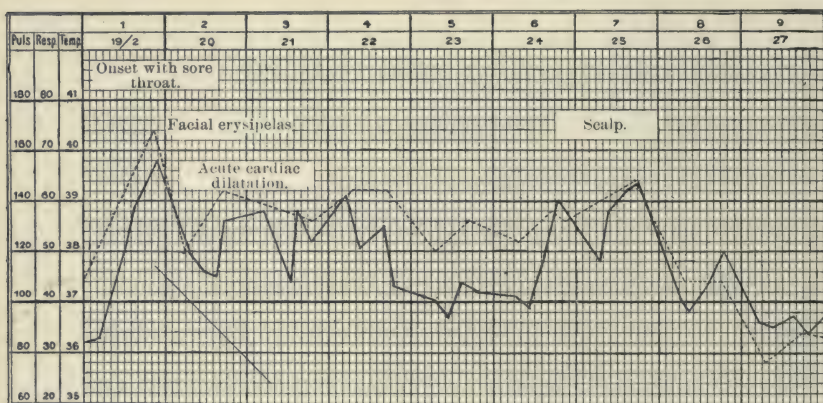
FIG. 23.

nomena and severe disturbances of the general condition may appear. Within a few hours, or after the lapse of one or two days, a severe coryza or a sore throat may follow, and shortly afterward the cutaneous eruption begins at the nostril or inner canthus. The inflammation of the mucous membrane is accompanied by active redness, swelling, violent local pain, and a markedly tender swelling of the submaxillary lymphatic glands. The redness is sharply outlined, as a rule, and the swelling is of varying grade. Sometimes inflammatory edema is present, for example, in the uvula, epiglottis, or aryepiglottic folds. The appearance of the pharynx is by no means characteristic, and scarcely to be differentiated from other varieties of severe sore throat. The true character of the disease is only surely recognized when the erysipelas appears upon the skin.

The following observation may serve as an illustration (Fig. 23):

G. Alwine, servant girl, æt. seventeen, just recovered from typhoid fever, and on the afternoon of the twenty-first day of convalescence, was
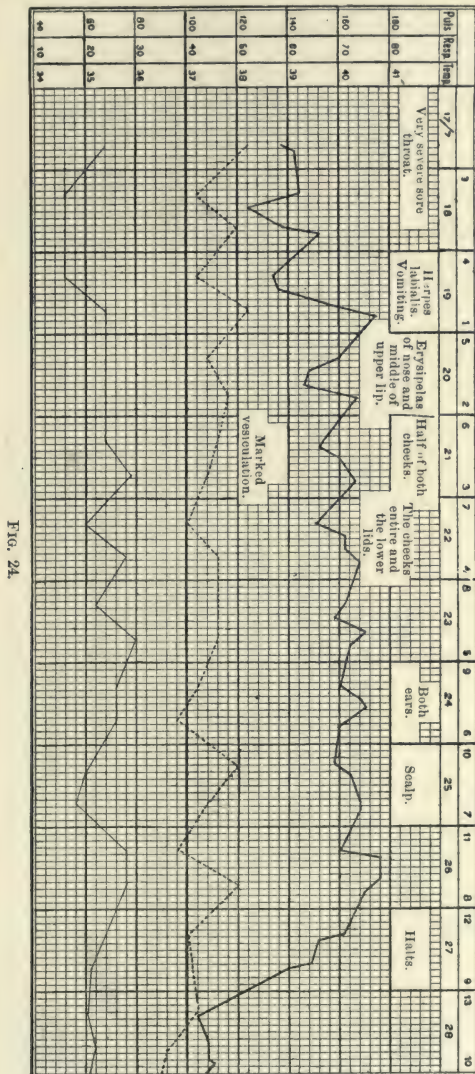
FIG. 24.

·suddenly attacked by a chill, headache, and pain in swallowing. A rapid rise of temperature to 39.8° C. (103.6° F.) followed, with a simultaneous increase of the pulse-rate from 90 to 168. A severe sore throat was pres-,ent with marked tenderness of the neck. During the next night an ery-

sipelas appeared, which proceeded from the interior of the nose (or from the sore throat) and attacked both cheeks symmetrically. These were very red, tense, painful, and tender. A marked dilatation of the heart, extending somewhat beyond the right sternal border, was present. This enlargement had also been observed during the typhoid fever, but it had completely returned to the normal three weeks before the erysipelas. It again remained until the temperature fell to the normal. The pulse was in the mean time rapid and frequently very fluttering.

The erysipelas attacked the entire face with the exception of the chin, and, after a pause of thirty-six hours, spread to the scalp. Bullæ and crusts were formed upon the face and ears. The patient completely recovered.

Both the beginning and the course of the disease may, however, be more violent, as is shown by the following case (Fig. 24):

Frieda R., æt. eighteen, servant girl. The disease began suddenly, July 16, 1897, with violent pains in the neck. Upon admission on the following day there was marked redness and swelling of the entire soft palate and of the lateral portions of the throat, especially upon the right side. The submaxillary glands were markedly swollen and tender. Severe local disturbances were also present.

The swelling in the fauces decreased until the afternoon of July 19th, when a rise of temperature and herpes labialis indicated a change for the worse.

On the morning of July 20th the entire nose and the middle portion of the upper lip were markedly red and swollen.

On July 21st the erysipelas spread symmetrically over the half of both cheeks and there was a pronounced formation of vesicles. The constitutional depression was profound.

On July 22d, after a very restless night, the cheeks and eyelids were completely involved.

On July 24th both ears were attacked. Daily vomiting.

On July 25th the entire scalp was affected.

On July 26th the disease commenced to disappear and the constitutional condition became better.

The next case is an example of the very even course of an erysipelas of the mucous membranes (Fig. 25):

A waterman aged seventeen had had violent pains in the neck and a chill two days before admission (July 13, 1896). In addition to redness and marked parenchymatous swelling of the fauces, he had an erysipelas which spread over the entire nose and both cheeks like a butterfly. No vesicles were present. Until the fifth day of the disease the erysipelas involved both eyelids and a portion of the forehead, covering the entire forehead upon the sixth day. On the seventh day the scalp was affected as far as the vertex, and on the ninth day the remainder of the scalp, with the exception of a small area in the occipital region, was attacked. Cessation and rapid resolution then followed. The general condition was never particularly disturbed.

The next chart (Fig. 26) also represents a fairly mild case, which

was characterized by the long duration of the phenomena connected with the mucous membranes:

H., a servant girl, æt. twenty-one, had already had one attack of erysipelas a year before. She again became ill August 14, 1893, with fever, a chill, and violent pains in the head and neck, which extended to the nose
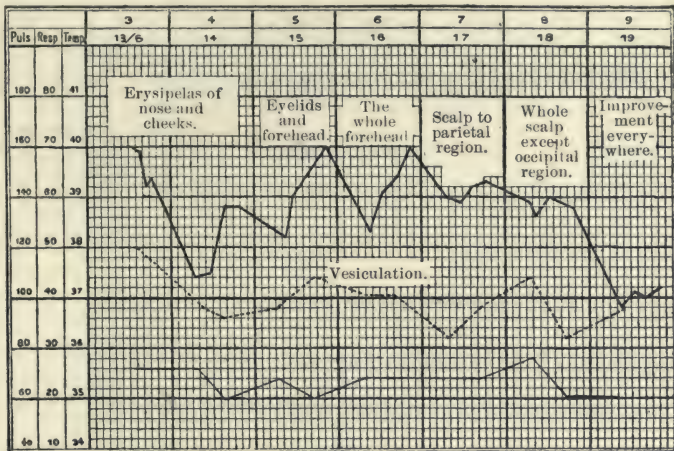
FIG. 25.
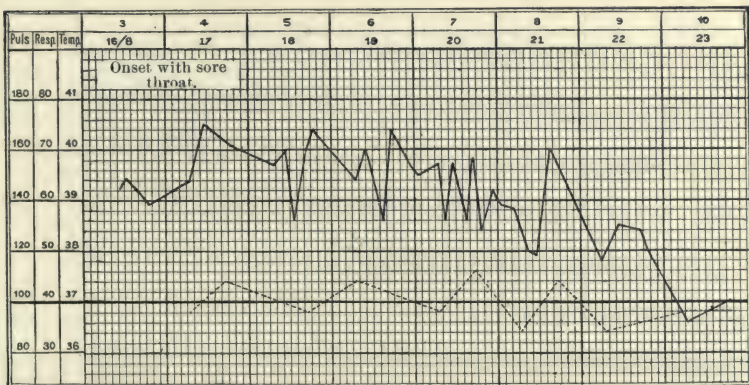
FIG. 26.

on the following day. Upon the third day of the disease there was redness and swelling of the tonsils; the nose was slightly reddened, but markedly tender to the lightest touch. Not until the morning of the fifth day was a distinct erysipelas of the nose and forehead observed, which extended to the scalp.

In all the previous cases the exanthem of the mucous membranes made its exit from the nose. This is usually the case. Much more

rarely the erysipelas makes its appearance from the mouth, nasal duct, or even from the internal ear.

Extension through the Nasal Duct.—The eruption spread from the right nasal duct in the following case:

F., a washerwoman, æt. twenty-two, suddenly became ill, on the day before admission (February 25, 1894), with violent pains in the neck, which rapidly extended into the nose and right eye. Upon admission she had a severe sore throat, conjunctivitis, and a beginning erysipelas of the eyelid, which involved the entire face upon the fourth day of the disease. The scalp was attacked upon the fifth, and the disease ceased upon the seventh day. A high remittent fever was present from the third to the sixth day of the disease; the temperature fell to normal upon the eighth day.

A similar case is reported by St. Philipp (*Gaz. méd. de Bordeaux*, Zuelzer):

A woman, aged twenty-five, was attacked by sore throat with swelling of the cervical lymphatic glands. Mucous membranes of the mouth edematous, numerous vesicles upon the palatine arch. Dryness and burning in the throat. After nine days a painful red point developed in the canthus of the right ear, from which extended a facial erysipelas.

Extension through the External Ear.—The immediate extension of a faucial erysipelas to the skin through the internal and external ear is still more rare.

Lennander[45] ("Schmidt's Jahrb.," 226, S. 139) saw two such cases. In the first, the faucial mucous membrane was purplish-red, tensely swollen, and there was a marked sensation of constriction. After lasting two days there was earache and a purulent discharge from the ear. Redness and swelling of the auricle and then a typical facial erysipelas quickly followed. As the disease advanced the inflammation subsided in the throat and ear.

We personally observed the following case:

M., shipwright, aged sixty-eight. Admitted March 13th, died March 14, 1897.

He was unconscious upon admission and had a suppuration of the left middle ear with perforation of the membrana tympani, from which an erysipelas had extended to the left auricle and cheek.

The autopsy revealed, in addition to the left-sided purulent otitis media and erysipelas, an edema of the left aryepiglottic fold (erysipelas?) and lobular infiltrations of both lower lobes.

Primary Erysipelas of the Larynx.—Erysipelas of the larynx is a much graver affection, and happily of rarer occurrence. The disease may be either primary or secondary. The latter is relatively more frequent, since a faucial erysipelas may not only extend upward,

but also toward the larynx. It is not unlikely that a class of cases which present the clinical picture of primary edema of the glottis should be considered as primary erysipelas of the larynx.

If the erysipelas spreads from the pharynx to the larynx, the transition to the aryepiglottic folds and to the epiglottis may usually be accurately followed. The affection is characterized by continuous fever, increased pain in swallowing, and not rarely by a rapidly threatened suffocation.

As a rule, the course of a primary laryngeal erysipelas is different. Here the disease may be introduced by a chill and fever lasting from one to three days, while no other symptoms may exist but non-characteristic pains in swallowing. At first there is not rarely a complete absence of any perceptible change in the pharynx. An active inflammation of the lymphatic glands soon follows, however, which is usually more marked upon one side than upon the other; the region in front of the thyroid cartilage is consequently very painful as a result of the lymphangitis. The remaining changes now become visible in the interior of the larynx, often making their appearance with alarming rapidity.

At first one mostly finds a circumscribed bluish-red edema in the glosso-epiglottic fossa, which always rapidly extends to the epiglottis and aryepiglottic folds. If the swelling of the epiglottis is marked and rapid, it is as disagreeable to the patient as we know it to be in laryngeal tuberculosis. Every attempt at deglutition is not only painful, but often impossible. The phenomena of stenosis of the larynx may now develop even within a few hours, and surely cause death if suffocation is not prevented by a timely, and in fact immediate, tracheotomy.

The erysipelas may remain in the larynx, and this is the more common occurrence. The picture then changes completely a few days after the threatening symptoms, since with the cessation of the erysipelas, not only the temperature falls, but complete resolution rapidly follows, as is the case in the skin.

If the erysipelas extends to the trachea, bronchi, and actual pulmonary tissue, there appear, in addition to severe subjective disturbances and pains along the trachea, a renewed high and continued fever, marked dyspnea, and more or less distinct symptoms of bronchitis, pneumonia, and pleurisy.

The following observation, which Ziegler[46] has reported from von Ziemssen's clinic, is very instructive.

A malarial patient, twenty-eight years of age, had completely recovered and was about to be discharged. On the morning of November 18th he again became ill with a chill and fever, which was at first regarded as a relapse of malaria. In the evening he complained of difficulty in swallowing, for which no objective cause was found. During the night the difficulty increased and there were violent pains in the left side of the neck. Temperature, 40° C. (104° F.). November 19th, 7 A. M., tissues of neck swollen upon the left side. Larynx very tender. Pharynx normal. In the left glosso-epiglottic fossa a livid swelling, the size of a bean, was seen to hang over the reddened epiglottis like a hood. At 11 A. M. the epiglottis was already bent like a saddle and the edema had so increased that the entrance to the larynx was entirely hidden upon the left side. The edema rapidly increased until a distinct laryngeal stenosis developed, which necessitated tracheotomy at 3 o'clock. The temperature fell to 38° C. (100.4° F.) in the evening, rose again to 39.3° C. (102.7° F.) upon the following day, and then fell to normal with a simultaneous·rapid disappearance of the inflammatory edema. The larynx was almost entirely normal by November 23d.

During the next five days there was a slight renewal of the fever with bronchopneumonic areas in the right lower lobe and a simultaneous return of an edematous swelling of the left arytenoid, which became larger than a cherry. Rapid and complete resolution then followed.

The observation of J. Herzfeld[47] is also of interest:

A lady, aged twenty-five, who had two days before passed through an attack of lacunar sore throat, still had pain in swallowing. Temperature, 39.8° C. (103.6° F.); pulse, 125; respiration, 45 and superficial. Laryngoscopic examination showed the epiglottis to be thick, swollen, edematous, and immovable; the arytenoids and the aryepiglottic folds were very edematous; it was impossible to see into the larynx. The voice was feeble and low, though not exactly hoarse. Marked tenderness in front of the laryngeal region.

In the next few days phlyctenular formations developed upon the epiglottis, and two of them suppurated. During this time there was an intermittent fever and great laryngeal tenderness. The redness and swelling then disappeared, the small ulcers healed, and complete recovery followed.

I myself observed the following case:

Mrs. R., aged twenty-eight, who had always enjoyed good health and never had erysipelas, became suddenly ill on the evening of February 10, 1898, with violent shooting pains in the neck. These were accompanied by increasing dyspnea, and became so severe that a physician was summoned. The patient was transferred to the hospital, and on the morning of February 11th such an intense redness and inflammatory edema of the epiglottis and the arytenoid mucous membrane was found that the entrance to the larynx was almost completely hidden. As much of the vocal cords as were visible seemed perfectly normal. The larynx was very tender to the touch. Temperature, 38.7° C. (101.7° F.); pulse, 110–120; respiration, 20. On February 12th the temperature varied between 38.4° and 39.5° C. (101.1° and 103.1° F.); the inflammatory edema at the entrance to the larynx had somewhat increased and the uvula was also

tensely swollen. Scattered petechial hemorrhages. Herpes labialis. General condition markedly disturbed. In the next two days the temperature fell and the swelling of the mucous membrane disappeared.

The epiglottis was still swollen and presented a shining, bloody appearance, as though it were japanned. The return to normal was not complete until February 23d.

There was no history of injury by portions of food or the like, and nothing of etiologic moment could be observed. Cultures were taken daily and revealed the presence of cocci alone. Streptococci were also found.

The profuse expectoration of a clear serous sputum, which varied in amount from 150 to 400 cubic centimeters, seems worthy of note.

According to Massei,[48] who first taught that primary laryngeal erysipelas was a uniform and independent disease, the affection may be epidemic and sporadic. He deemed it advisable to differentiate between a form with constitutional symptoms, and another, with preponderating local disturbances. The former is characterized by the appearance of pneumonic areas, and usually by a fatal termination; the latter form is distinguished by the laryngeal stenosis and dysphagia, and usually ends in recovery.

It is not unlikely that the majority of the cases which have been described as cases of primary edema of the larynx belong to this category.

In addition to Massei and Ziegler, A. Bergmann[49] especially has reported instructive cases. Massei lost only 2 out of 14 cases (some of them evidently light); one of Bergmann's cases was tracheotomized, both recovered; of Fasano's two cases, one died.

An observation of Gerling[50] makes it likely that laryngeal erysipelas, like cutaneous erysipelas, may lead to manifold transmissions. Gerling treated a girl with facial erysipelas, who also had an active laryngeal inflammation and hoarseness. The three younger sisters of the patient had been attacked at the same time by a laryngeal erysipelas, while the face remained free. The disease was characterized by high fever, marked hoarseness, croupy cough, dyspnea, and stridor. They all died in from one to three days. At the autopsy, which was allowed only in one case, an intense inflammation of the larynx was the only morbid condition found.

Extension to the Bronchi and Pulmonary Tissue.—The bronchitis produced by the extension of an erysipelatous inflammation offers no distinguishing characteristic; its rapid appearance and disappearance, however, sometimes speak for an erysipelatous origin.

The same is true of the pneumonia, which, as a rule, is to be re-

garded as erysipelatous only when it has arisen in immediate connection with a cutaneous, pharyngeal, or laryngeal erysipelas.

Many observations, however, allow of the supposition that a primary erysipelatous pneumonia may arise without a preceding erysipelas. The following case may be quoted as an example:

Mosny[51] (Sur un cas de bronchopneumonie érysipélateuse sans érysipèle) saw a pneumonia appear in the servant of a gentleman suffering with facial erysipelas, which terminated fatally within two days. At the autopsy, a circumscribed bronchopneumonic area was found, from which pure cultures of streptococci were obtained. These produced a true erysipelas in the ear of a rabbit.

In a case of pneumonia occurring in the course of an erysipelas, Denucé[52] found the specific cocci both in the small blood-vessels and capillaries of the lung, and also in the pericardial and pleuritic exudates. Schönfeld[53] made a like observation in a pneumonia of similar origin.

If, in such cases, the connection of the fatal pneumonia with the erysipelas can be proved etiologically and bacteriologically, we may only suspect that the so-called "wandering pneumonias" are instances of masked erysipelas.

Waldenburg[54] and Friedreich[55] have very definitely emphasized the connection between these peculiar forms of pneumonia and erysipelas. According to them, wandering pneumonia is characterized by the frequent change of the hepatized districts and the rapid resolution of previously affected areas. The disease has a marked tendency to affect also the opposite lung. From the first advent of the hepatization until its disappearance only two or three days may elapse, so that the resemblance to the course of wandering erysipelas is very strong. The duration of the disease depends upon the size of the affected region and upon the rapidity of the advance. It may last for several weeks, as does a universal erysipelas migrans. The temperature curve is very irregular, and may correspond to those already given in cases of wandering erysipelas of the skin.

According to Friedreich's statements, a marked splenic swelling is uniformly present; it is much larger and far more common than is usually the case in croupous pneumonia. The sputum is very rarely "pneumonic," usually simply catarrhal, although distinct condensed portions are demonstrable. Albuminuria is said to occur with the same frequency as in cutaneous erysipelas.

The above-mentioned peculiarities, of which the serpiginous advance of the hepatization, the marked tendency to bilateral involve-

ment, the uniform occurrence of a palpable splenic tumor, and the frequently observed coincidence with cases of acute erysipelas and puerperal fever deserve to be especially emphasized, caused N. Friedreich to designate such forms as "erysipelatous pneumonias."

"Only from individual diversities of structure of the various organs, and their consequent varying predispositions to disease, can we understand, in a measure, that one and the same infectious substance distributed throughout the entire body can sometimes cause erysipelas of the face, sometimes pneumonia, and again inflammation of the pharynx."

Far be it from me to deny the possibility of such primary erysipelatous pneumonias. I may, however, be allowed to say that they are extremely rare, still rarer than primary laryngeal erysipelas. The points above stated, especially the serpiginous course and the tendency to bilateral involvement, are not sufficient to support the supposition that a pneumonia is erysipelatous (caused by streptococci), since the diplococcus of Fränkel may be the only organism found in such cases. It is certain, however, that such pneumonias can be caused by the streptococcus when they accompany or follow an external erysipelas and show all the previously mentioned clinical characteristics. It may remain doubtful whether a direct transmission of the germ from the skin to the lungs has caused the inflammation, or whether the infection has occurred through the blood. In the latter case the erysipelatous pneumonia is to be simply interpreted as a septicemic manifestation. We will consider the septic affections later in our article.

We have already mentioned the fact that the erysipelas may travel in the opposite direction, since it may extend from the skin to the mucous membranes through the natural orifices of the body. This has also been certainly recognized and described by Gubler and Trousseau.

Contrary to the general teaching, König[56] believes that this secondary pharyngeal erysipelas is more frequent than the primary. We cannot agree with him, since the opposite obtains from our clinical material.

The wandering of the erysipelas into the pharynx almost always takes place through the nose. It may occasionally occur through the mouth, in which case a true erysipelas of the tongue develops, which is characterized by redness, swelling, and pain, and which may lead to serious symptoms if the edema is excessive.

Secondary erysipelas of the genital mucous membrane will be fully discussed in the following section.

Erysipelas of the Mucous Membrane of the Female Genital Tract.—In the introduction we have already traced the intimate relations existing between erysipelas and puerperal fever. It has been shown that a fatal puerperal sepsis may be caused in recently delivered women by physicians and nurses infected with erysipelas. The proof of the identity of the exciting cause of the two diseases made these apparently surprising observations quite intelligible.

The puerperal patient is exposed to the danger of erysipelas in a far greater measure than other women. Infection always occurs at the external genitalia, where the numerous smaller and larger lacerations of the mucous membrane offer points of entrance for the streptococcus. The disease not rarely begins with a chill, minute inspection of the genitals failing to discover the outbreak of the erysipelas. In other cases there are simultaneous swelling and redness of the vulva. At all events, the character of the disease is recognized on the second or third day of the fever, by the sharply outlined border of the erythema as it spreads from the vulva to the surrounding tissues. The swelling of the labia may reach so extreme a degree that superficial necrosis occurs. Violent pain is usually present, and is indicative of the extension of the disease.

Erysipelas proceeding from the genitals may extend upward to the nates, back, and abdomen, downward to the lower extremities, or in both directions.

More important, however, is the extension of the erysipelas to the internal genitals. The conditions for such an occurrence are, again, much more favorable in puerperal than in other women. In such cases the disease often advances with frightful rapidity, and the rapidly following peritoneal symptoms indicate that the infectious germs have already wandered through the uterus and tubes. The soft and spongy mucous membrane does not offer the least resistance to the stormy attack; the culture-medium, on the contrary, favors the increase of the bacteria to an unusual degree, since the lymph paths and the veins are more dilated than in non-puerperal women.

A sure diagnosis of "grave internal puerperal erysipelas" (Virchow), however, can rarely be made. According to my opinion, it is probable only when a puerperal woman develops a distinct erysipelas of the vulva and has violent pains in the lower part of the abdomen and other peritoneal symptoms.

This was the case in the following personal observation (Fig. 27):

Minna W., servant girl, aged twenty, was admitted March 7, 1893, with coma and eclampsia (albumin 12%). She was rapidly and naturally

delivered of a putrid fetus; the placenta came away after about sixteen hours (Credé).

The coma had disappeared and the patient felt entirely well on March 9th. The amount of urine daily secreted arose to 1200 c.c.; the albumin present fell to 1%.

March 10th, swelling and marked sensitiveness of the labia, no marked redness present. Lochia have no bad odor.

March 11th, general change for the worse. Cough. Pain on the right side, low down, and posteriorly.

Upon the morning of March 12th a distinct erysipelas in the neighborhood of the vulva with increased swelling of the labia was observed.

During the following days the erysipelas extended upward to midway between the navel and the symphysis, and downward as far as the middle of the thigh. There was also a marked hypersensitiveness of the abdomen, which was more diffuse than the area of external erysipelas. During
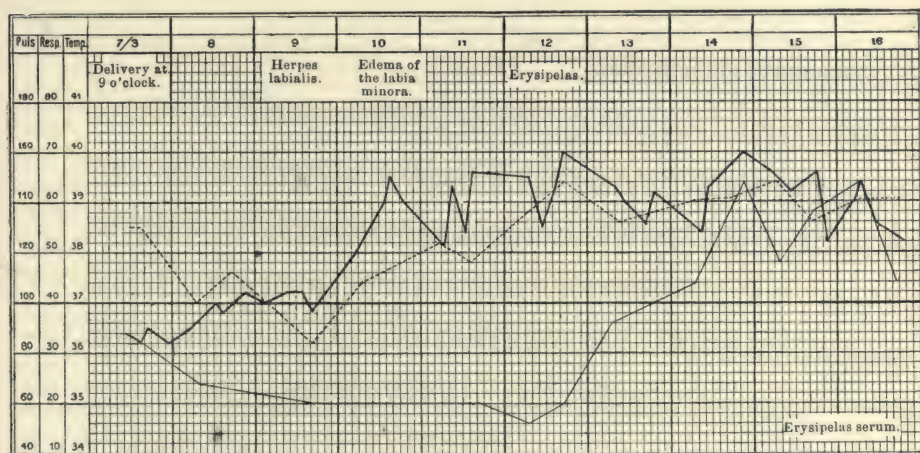
Fig. 27.

the two days before death injections of Emmerich's serum were made without any effect whatever.

The autopsy revealed, in addition to the remains of the external erysipelas, a marked inflammation of the mucous membrane of the vagina and uterus, numerous small intramuscular and subserous abscesses in the uterus, and a recent general fibrinopurulent peritonitis.

We once saw an erysipelas extend from the trunk into the rectum. The entire rectum was greatly swollen, the mucous membrane intensely reddened and in parts showing a bluish discoloration.

(d) CONCOMITANT PHENOMENA AND SEQUELS OF ERYSIPELAS.

Cerebral Symptoms.—Among the concomitant phenomena of erysipelas, the disturbances of the cerebral functions certainly occupy the most prominent place. In addition to headache, which is almost never absent in erysipelas of the face and scalp, unrest and mild

delirium are of rather usual occurrence. Lethargy and coma also occur with such frequency that it is not necessary to immediately give an unfavorable prognosis, when the sopor is even of long duration.

The delirium is by no means in direct proportion to the height of the fever or the extent of the disease, although cases are sometimes seen in which such is the case. It does seem true, however, that delirium is far more frequently observed when the scalp is attacked.

Traube[57] explained the frequency of the delirium in cases of erysipelas of the face and scalp by the fact that, in addition to the general influence of the fever, a considerable irritation was present in the area supplied by the trigeminus, "the sensory fibers of which, from the shortness of their course, may transmit impulses from the periphery with the least loss of intensity."

The differentiation of these cerebral symptoms from an actual meningitis is by no means easy in the individual case, especially since lumbar puncture may also fail to clear up the situation. We have an example in the following observation:

W., trader, aged forty-four. Admitted September 14, 1896; died September 16, 1896.

The companion of the comatose patient stated that the disease had existed for five days.

A bulbous erysipelas of the left auricle and scalp was observed, as well as a purulent otitis media with almost complete destruction of the left membrana tympani. The pupils were contracted and immobile; marked restlessness, carphology, and the neck sensitive to pressure. Temperature, 40° C. (104° F.); pulse, 100; respiration, 20.

During the next day the condition remained unchanged. Lumbar puncture under a pressure of 250 millimeters yielded a cloudy serous fluid rich in leucocytes, free from bacteria. The removal of 20 c.c. caused no change.

Death occurred on the following day, the temperature being 41.3° C. (105.3° F.).

Autopsy: Purulent otitis on the left side with suppuration in the mastoid cells. General purulent cerebrospinal meningitis. Cloudy swelling of the heart muscle and of the kidneys.

Pure cultures of the Staphylococcus pyogenes aureus were obtained from the pus from the ears, and also from the meningeal suppuration. The lumbar fluid had remained sterile.

In spite of the negative result of the bacteriologic investigation of the spinal fluid, the diagnosis of meningitis had scarcely been doubted, since there was profound coma with permanently immobile pupils.

In this case it remained undecided whether it was a primary erysipelas with a subsequent perforative otitis, or whether the erysipelas was engrafted upon a preceding otitis media. The latter supposition is the more likely.

Retrobulbar inflammation and purulent infiltration of the orbital areolar tissue are rare, though not unknown. If retrobulbar inflammation occurs early, shortly after erysipelas has attacked the lids and produced an acute intense edema in this situation, the delirium present may be wrongly interpreted. In the case now to be described we considered secondary meningitis to be the most likely diagnosis. At the autopsy, however, we found, in addition to purulent infiltration of the orbital areolar tissue and thrombosis of the transverse and cavernous sinuses, only a circumscribed purulent basal meningitis.

R., a brakeman, aged forty-one years, was admitted at noon, July 14, 1897, in a completely unconscious condition and died on the evening of the following day.

The entire face was edematous. Both eyelids (especially the left) swollen and markedly protruding; conjunctiva also very edematous. Marked redness over the swollen area and tendency to the formation of crusts. The erysipelas extended to the forehead.

The unconsciousness continued without change. The temperature varied between 37.6° and 39.8° C. (99.6° and 103.6° F.). Pulse about 140. Respiration rapid and stertorous. The autopsy revealed the above-mentioned condition.

This termination is rare, however, as is shown by the sanitary report of the Royal Prussian Army.[58] Out of about 1500 cases of erysipelas reported from 1890 until 1892, there are only two instances of a "purulent meningitis from an extension of the inflammation along the sheath of the optic nerve."

The retrobulbar inflammation is also dangerous when it does not extend to the meninges and sinuses, since those cases which recover are, as a rule, blind in the affected eye.

Knapp was able to collect 37 cases of this form of blindness (*von Graefe's Archiv*, Bd. xiv, 3. Heft). A complete atrophy of the optic nerve almost constantly results. A temporary blindness may, however, be followed by a complete return of the visual power, as is proved by the following case.

In a sixteen-year-old servant girl, who had become blind four days after the beginning of a facial erysipelas, Weiland[59] found the eyeball insensitive and free from pain upon pressure and motion. The pupil was somewhat dilated and reacted normally to light. The papilla was opaque with an atrophied border. Vessels small. Complete amaurosis. Recovery ensued after two weeks' treatment by sweating.

Concomitant Phenomena in the Respiratory and Circulatory Organs.—In addition to the forms of pneumonia which might be designated as actual erysipelatous concomitants in the respiratory

and circulatory organs, there may occasionally appear croupous pneumonias of the ordinary variety and lobular areas of inflammation produced by inspiration. The latter form particularly obscures the prognosis. They occur only in the severe cases with marked disturbances of consciousness, and in cases of wandering erysipelas of long duration.

Changes in the circulatory organs are not rare. We have already mentioned a case (page 463) in which a considerable dilatation of the heart was present during the febrile period. Such an observation is, however, of rare occurrence. We rather frequently find soft blowing murmurs at the apex or over the entire heart, which may, under certain circumstances, be due to endocarditic processes. It cannot be doubted that an acute endocarditis may be caused by erysipelas alone, and that it may occur in previously healthy valves or as a recurrent form of an existing valvular lesion. The differentiation of an endocardial from a febrile murmur is as difficult as in acute articular rheumatism, and, as a rule, we are able to form a definite opinion only after long observation. A valvular lesion may undoubtedly follow such an acquired endocarditis.

Pericarditis is of rare occurrence, and is usually the result of an endocarditis or of other sequelæ of erysipelas which will be considered later.

Irregularities of the heart's action are not uncommon; they may be dependent upon disturbances of innervation or muscular weakness. In the latter instance, they have a graver significance and demand careful study, because life may be endangered, not only during the actual course of the disease and febrile period, but also during convalescence. This is taught by the following records, which are worthy of careful consideration:

J., a workman, aged fifty, came to us January 18, 1897, with a facial erysipelas that was undergoing resolution. On the following day the temperature was normal and he seemed about to make a good convalescence. At times, however, the pulse was still weak. He died suddenly on January 24th, *i. e.*, on the fourth afebrile day. The autopsy revealed an embolus of the pulmonary artery, although the most careful investigation failed to reveal traces of thrombi in the heart or at any place in the venous system.

Two weeks after the beginning of a facial erysipelas in a lady forty years of age, Traube[57] (page 579) saw an attack of impaired respiration with a marked sensation of pressure within the chest. Such attacks were repeated; the lips were pale, the face was anxious, the pulse was small and rose to 140. After some days a dark brownish-red expectoration surely indicated the presence of infarcts, which Traube considered to be

dislodged thrombi that had formed in the right heart. Recovery ensued after many weeks.

In another case he observed an entirely unexpected death from cardiac paralysis, on the thirteenth day of an erysipelas in "an unusually fat gentleman of sixty-four years."

[Examination of the blood in a streptococcus disease like erysipelas might naturally be expected to reveal leucocytosis, and as a matter of fact this condition is generally present, particularly in severe cases and in those which are accompanied by suppuration. In 1871, Virchow * pointed out that an acute irritation of the glandular apparatus led to leucocytosis. It becomes serious in "wandering erysipelas" when this form of the disease attacks debilitated persons.]

Concomitant Cutaneous Phenomena.—We have already touched upon the fact that subcutaneous abscesses may develop in the immediate train of a cutaneous erysipelas. They may occur upon the head, trunk, or extremities, and rarely attain a large size. Several abscesses may occur simultaneously or shortly after each other, in the same patient, and in different parts of the body. They almost exclusively occur in areas which have been involved by the erysipelas. In our 140 cases they were observed 9 times, *i. e.*, in 6.1% of the total number; in 4 of these 9 cases the abscess was located in the eyelid.

They are generally of no great importance if opened at the proper time. Pure cultures of streptococci are usually obtained from the pus; in 3 cases we found staphylococci exclusively. This was undoubtedly due to a secondary infection of the encrusted cracks in the skin.

Far graver is the development of more or less extensive phlegmonous inflammations, which appear more frequently in the extremities and lower portions of the back than in other situations. They may arise without mixed infection, and are due to the entrance of streptococci into the deeper layers of the tissues or into the circulation.

Internal suppurations may likewise be produced by the streptococcus. The origin of a purulent arthritis of the knee (Hoffa[28]) and the occurrence of a purulent meningitis have both received our attention. A purulent meningitis may even be associated with a cerebral abscess, as is shown in the following case from the "Sanitary Report" for the years 1884–1888:

A circumscribed fluctuation was observed above the left eyebrow of a soldier suffering from facial erysipelas. Rough bone was found upon opening the abscess; two similarly affected areas were discovered in the parietal bone. Death occurred with symptoms of paralysis. The au-

* *Cellular Pathology*, 1871, p. 230.

topsy showed that the bone in the affected areas was infiltrated with pus and revealed an abscess as large as a pigeon's egg in the anterior portion of the frontal lobe.

Gangrene, Suppuration of Glands, Purulent Edema.—The development of cutaneous gangrene is also one of the dangerous complications and sequelæ of erysipelas. Those places are particularly endangered in which the skin lies immediately upon a bone without an intervening cushion of fat. The necrosis may be only superficial and circumscribed, or it may affect the entire skin over a large area. Although the life of the patient may be spared, the disease may be followed by serious impairment of function. Such gangrene is observed not only in elderly individuals, but also in men in active adult life. Extensive gangrene is nevertheless very rare. In the "Sanitary Reports of the Royal Prussian Army" for the years 1890–1892, there were only 4 cases of cutaneous gangrene out of 1491 cases of erysipelas; between 1884 and 1888 there were 4115 cases of erysipelas, with likewise but 4 cases with severe gangrenous inflammations.[60] The following instructive cases are quoted:

1. A soldier with an abrasion at the knee developed an erysipelas which rapidly extended to the hip. On the eighth day of the disease several bluish spots and vesicles filled with cloudy serum developed. A large gangrenous slough involving one-fourth of the affected skin was finally cast off. Death from exhaustion followed after four weeks.

2. General cutaneous erysipelas of the entire body from a fistula following a resection of the knee. Extensive gangrenous destruction of the scrotum and gangrene of the resected joint. After the soft parts had sloughed from the knee, the commencing bony union was dissolved and an amputation of the extremity was performed. Recovery. ("Sanitätsbericht," 1895, page 28.)

In a girl of twenty-two, I myself saw necrosis develop in the parietal bone on the fifteenth day of the disease. The necrotic area was as large as a dollar or a five-shilling piece. Complete recovery ensued after the separation of the sequestrum. The history of this case will be fully given in the section on Treatment.

The inflamed lymphatic glands produced by erysipelas may suppurate at the same time that the subcutaneous suppuration or cutaneous gangrene develops. This happens only when subcutaneous abscesses or other sequelæ have previously developed in the affected skin. Although the staphylococci may at times gain an entrance to the tissues, the suppuration of the lymphatic glands may also occur without a mixed infection. If the patient is already weakened by an erysipelas such suppurations may endanger his life.

Death occurred in one of our patients on the twentieth day of the disease, as a result of the processes just described.

D., servant, aged fifty-three, was admitted October 5, 1893, with an erysipelas proceeding from an ulcer of the leg. She had irregular fever, which mostly showed remissions of 1.5° C. (2.7° F.). A circumscribed superficial gangrene developed in the skin over the patella and the inguinal glands suppurated. The autopsy revealed no other changes.

The development of a purulent edema is still more dangerous. It was formerly doubted that such a process could hold any relation with true erysipelas, and in modern times it has been considered necessary to ascribe such a purulent edema to a mixed infection. The old idea is certainly wrong; the modern one is only sometimes justified. There can be no doubt that an acute purulent edema may appear in an erysipelatous patient without the invasion of other varieties of bacteria. This is taught by the following case:

M., blacksmith, aged forty-six, strongly built and well nourished, was admitted March 12, 1890, in an unconscious condition. He had typical erysipelas with the formation of vesicles involving the face and right ear. On March 12th and 13th the temperature varied between 38.5° and 40.0° C. (101.3° and 104° F.). On March 14th the temperature fell spontaneously to 37.7° C. (99.9° F.), and a normal retrogression followed until March 15th, when the morning temperature was 37.0° C. (98.6° F.).

In the course of the day the temperature again rose to 38.7° C. (101.7° F.), and a marked swelling and redness, with violent pain on motion, developed in the right arm and right leg. Death in collapse occurred on March 16th.

The autopsy revealed cloudy swelling of the liver and kidneys; no changes in the spleen or other organs. Incisions into the arm and leg showed marked edema but no suppuration. The intermuscular septa were partly necrotic; much seropurulent fluid flowed from every incision. This fluid contained streptococci exclusively, which were obtained in pure culture.

The transition to a general fatal sepsis is very rare, apart from the forms of puerperal erysipelas already described. The consideration of these processes will be found in the section upon septic diseases.

The following observations are added for the sake of completeness:

1. Kl., a strongly built female child, aged five months, was suddenly attacked with vomiting and fever, eight days before admission, and was said to have had swelling of the labia and redness of the back upon the following day.

Upon admission, September 17, 1898, the child seemed very ill. There was general anasarca with an indistinct erythema of the buttocks. The urine contained rather a large number of hyaline casts and considerable albumin. Just above the right elbow there was a more marked swelling and tenderness to pressure. The temperature is shown in figure 28.

On September 19th there was a distinct erysipelatous area, twice as large as the palm of the hand, which extended upward and downward from the labia. Some isolated spots with irregular, sharply outlined, elevated borders were also seen in the neighborhood of both knees.

FIG. 28.

On September 21st the erysipelas had extended over the abdomen as far as the umbilicus, and upon the anterior surface of the thigh as low down as the knee.

On September 22d the abdomen was involved up to the ribs, the skin of the back as far as the neck, and the lower extremities to below the knees.

On September 23d both legs were affected.

On September 25th only the anterior cervical region remained free; both arms were attacked.

On September 26th a general retrogression of the exanthem was observed; the inflammation was active only upon the forearms and legs.

On September 27th the hands and the right foot were attacked; the erysipelas stopped at the ankle upon the left side.

On September 28th an abscess above the right elbow-joint was opened. It occupied the position of the painful swelling previously observed. Cover-glass preparations showed masses of streptococci, many of them being intracellular. Cultures made from the pus revealed streptococci exclusively.

On September 29th there was striking dyspnea and a dulness low down on the right side and extending posteriorly. Aspiration yielded pure pus of the same nature as that in the abscess. Death at 6 P. M. Cover-glass preparations of the heart's blood were made the next morning, and showed numerous streptococci.
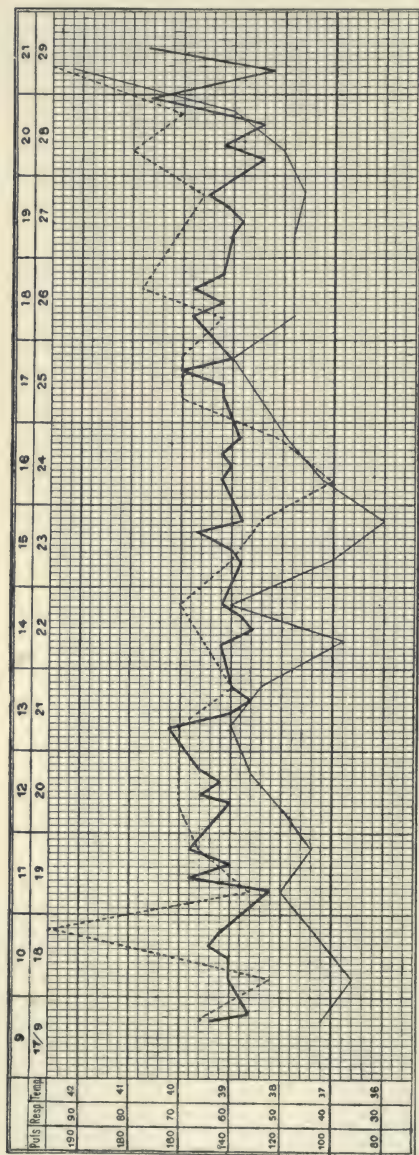
The autopsy revealed a small purulent exudate in the right pleural cavity, a purulent peritonitis with slight exudation, a soft enlargement of the spleen, severe nephritis, and a circumscribed abscess alongside of the right biceps. Nothing but streptococci grew in the cultures taken from the pleuritic and peritoneal pus, from the abscess, and from the blood.

2. Caroline L., tailor's wife, aged forty-four, was brought to the hospital January 17th in a semiconscious condition. She had been attacked four weeks before by an erysipelas of the face and scalp. One week before admission her joints became painful. Her face still showed extensive typical desquamation. Several joints were swollen and painful upon movement and pressure. There was distinct fluctuation in the knee-joint. In the pus, removed aseptically, masses of streptococci were seen, even without oil immersion, and they grew exclusively in the cultures. Nothing but streptococci grew in cultures taken from the urine and blood, and 254 colonies were obtained from 1 c.c. of the latter. A purulent choroiditis developed within a few hours, the coma increased, and the patient died twenty-four hours after admission.

The autopsy revealed, in addition to manifold suppurations of the joints and a right-sided purulent choroiditis, a soft splenic swelling with hemorrhagic infarcts and small purulent deposits and hemorrhages in the kidneys. Numerous streptococci were seen in cover-glass preparations of the blood from the dead body, and 160,000 colonies grew from 1 c.c. of this fluid.

Suppuration in the Frontal and Maxillary (Antrum of Highmore) Sinuses.—Violent frontal headache, following an erysipelas and persisting for weeks, must lead to the thought that inflammatory processes have developed in the frontal sinus as a sequel of the erysipelas. The supposition is particularly well founded when the facial erysipelas has proceeded from the throat or nose. A careful rhinoscopic examination may materially support the diagnosis.

In a case reported by Luc,[61] a suppuration developed in the antrum of Highmore and was undoubtedly due to a preceding facial erysipelas. Under strict aseptic precautions the antrum was opened through the canine fossa and cultures made which revealed nothing but streptococci. Two weeks later a fresh facial erysipelas developed, proceeding from the left nostril.

It is worthy of note that in this case the pus was absolutely odorless, while in the suppurations of the antrum, which frequently proceed from carious teeth, a bad odor is rarely absent. Here the first two malars were intact, although they usually contain cavities in such cases. It was this condition which led to the careful bacteriologic examination.

Suppuration in the Parotid Gland and in the Middle Ear.—Parotitis is in general very rare in erysipelas. In our 140 cases the suppurating form was observed but twice.

A far more frequent complication is otitis media, which is observed both after erysipelas of the external ear and also after pharyngeal erysipelas. We have already mentioned that the latter form may extend through the middle and external ear and appear upon the skin. It is particularly in these cases that the danger of meningitis exists.

Acute nephritis occurs rather rarely in erysipelas, while febrile albuminuria is common. In our 140 cases, acute nephritis was observed seven times, *i. e.*, in 4.7%.

Wagner[62] saw a case of nephritis, aggravated by delirium tremens, which died upon the third day.

The following case, admitted to my hospital, also suffered an acute death.

Franz E., butcher, aged twenty-two, four days before admission was attacked by violent pains in the neck, and two days later an erysipelas of the nose and cheeks followed. In addition to the erysipelas, the semiconscious and highly febrile patient had a severe acute nephritis (March 23, 1897). He died at the beginning of the seventh day of the disease (March 26, 1897). The erysipelas had involved the face and left ear. The urine was passed into the bed by the comatose patient.

Autopsy: In addition to the remains of the facial erysipelas, the cervical lymphatic glands were enlarged to the size of beans. There were several small abscesses in the left tonsil. The mucous membrane of the base of the tongue and of the pharyngeal and laryngeal orifices was discolored bluish-red. Marked tracheitis. Acute parenchymatous nephritis. Punctiform hemorrhages in the pelvis of the right kidney.

It is an interesting fact that an acute nephritis may repeat itself when a relapse of the erysipelas occurs. This is shown in the following case:

Andreas I., servant, aged twenty-six, was treated by us from January 19 until February 2, 1893, and from the 5th until the 27th of November, 1893, both times for fairly mild attacks of facial erysipelas. During his first visit the acute hemorrhagic nephritis was of seven days' duration. The second time it lasted for six days, but traces of albumin were found in the urine for ten days longer. In the last five days the urine was absolutely free from albumin or morphologic elements.

The erysipelatous recurrence had commenced with a violent sore throat, and had then appeared at the inner canthi of both eyes.

[Kirkbride has noted the presence of leucin and tyrosin in the urine in one case of erysipelas. These substances are products of the decomposition of proteids, and their presence implies a marked disturbance of metabolism.]

3. RELAPSES AND RECURRENCES OF ERYSIPELAS. HABITUAL ERYSIPELAS.

In no acute infectious disease is the tendency to recur so great as in erysipelas. Sometimes we see the erysipelas break out afresh within several days or weeks of its disappearance; sometimes months or years may intervene between the first and the following erysipelas. In the first instance it is likely that the pathogenic bacteria were still present in great number and virulence, and that they were excited to renewed activity by some trivial cause; in the latter instance, an entirely new infection may have occurred in an individual predisposed to the disease. Concerning these points we can only indulge in supposition, but our understanding of recurrences in general is facilitated by the frequency of early relapses, since we are justified in assuming that recovery from an attack of erysipelas, be it ever so severe, confers absolutely no immunity.

From a practical standpoint, we designate the repetition of the disease soon after the first attack as a "relapse" ("rechute" of the French), and the return of the same disease after several months or years as a "recurrence" ("récidive"). To the latter group belong the cases of so-called habitual erysipelas, that affect certain persons for many years, especially in the spring and autumn.

The relapse may sometimes appear after an afebrile intermission of but one or two days. It usually begins with active fever, and although the exanthem may occur simultaneously, it more frequently appears several hours or even a day later. The erythema ordinarily proceeds from an area previously attacked or from its immediate neighborhood, and then progresses with a similar or increased violence. It is by no means rare for the relapse to have a stormy beginning and then rapidly disappear with an insignificant eruption.

This is demonstrated in the following case (Fig. 29).

B., bricklayer, aged twenty-six, had an erysipelas that proceeded from the nose and involved the entire face and neck. The temperature fell to normal upon the sixth day of the disease. An afebrile period of two days then followed, during which he felt entirely well. The next morning he had a chill, the temperature suddenly rose, and in the evening the erysipelas again appeared upon the cheeks. Within two days the temperature was again normal and the erysipelas, which had only involved the cheeks, was fading away.

The next curve, figure 30 (Mrs. B.), shows the beginning of a relapse after an afebrile period of four days. The exanthem developed almost simultaneously with the increase in temperature, and started in the neck, up to which point the erysipelas had extended in the first attack. The

FIG. 29.

FIG. 30.

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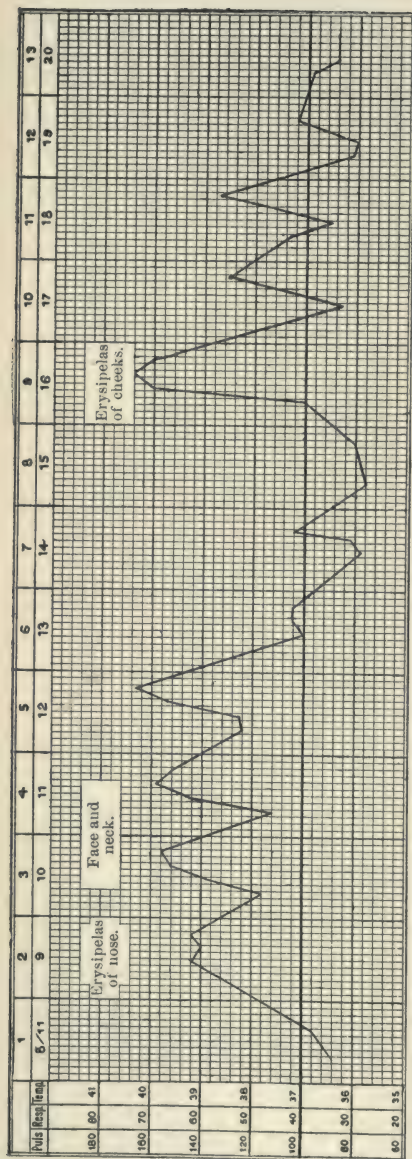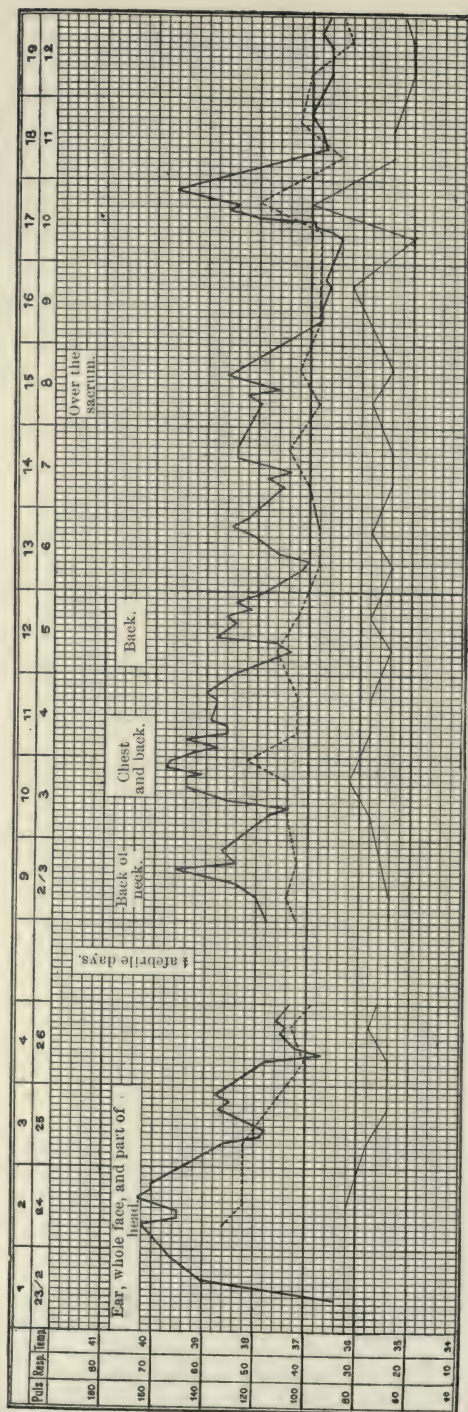
further course of the disease was mild, but nevertheless weakened the fifty-year old patient by its duration and great extent. The rise of temperature on the seventeenth day could only be explained by the last erysipelatous area over the sacrum.
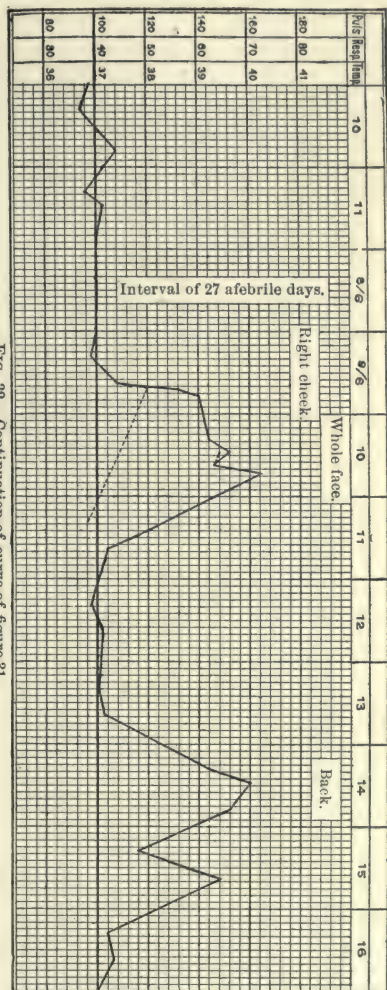
Fig. 31.

Fig. 32.—Continuation of curve of figure 31.
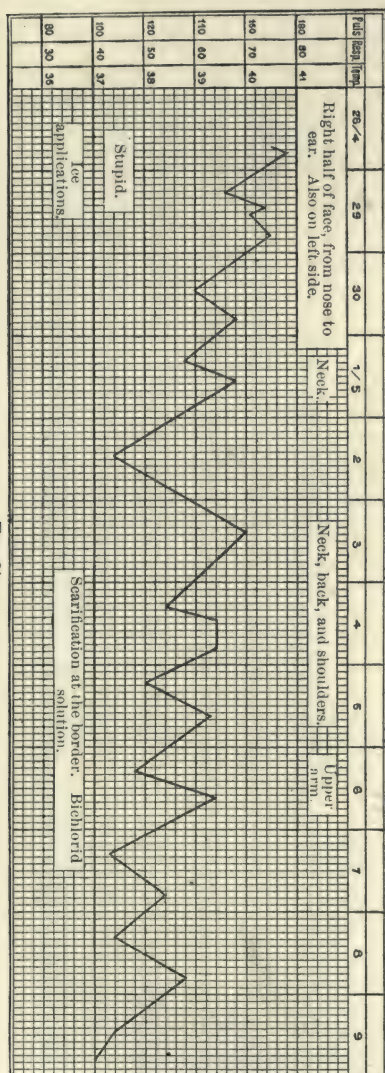
O., servant girl, aged thirty, had an erysipelas which within twelve days involved the face, neck, upper part of the back, shoulder, and arm. After an afebrile period of twenty-seven days, she had fever for three days (39°–40° C.,—102.2°–104° F.), and a relapse of the facial erysipelas. After

another afebrile period of two days, the fever reappeared for two days longer (40° C.—104° F.) and an exanthem developed upon the back. (Figs 31 and 32.)

Sometimes only a local relapse without any elevation of temperature may occur. Here the diagnosis must be made with caution. I have already expressed a certain amount of skepticism concerning the large number of afebrile cases in Roger's series of observations. A similar opinion must be held of Frickhinger's[14] collection of cases, from the first medical clinic of the Munich Hospital on the left bank of the Isar, in which 18% of the primary attacks and 24% of the recurrences are reported as afebrile. When we consider that the recurrences are often accompanied by only a temporary fever, it is not surprising if many cases are regarded as afebrile that have probably had fever two or three days previously.

The erysipelatous relapse may occasionally affect exactly the same cutaneous area that was involved in the primary attack. This occurred in the boy whose temperature chart is here given (Fig. 33).
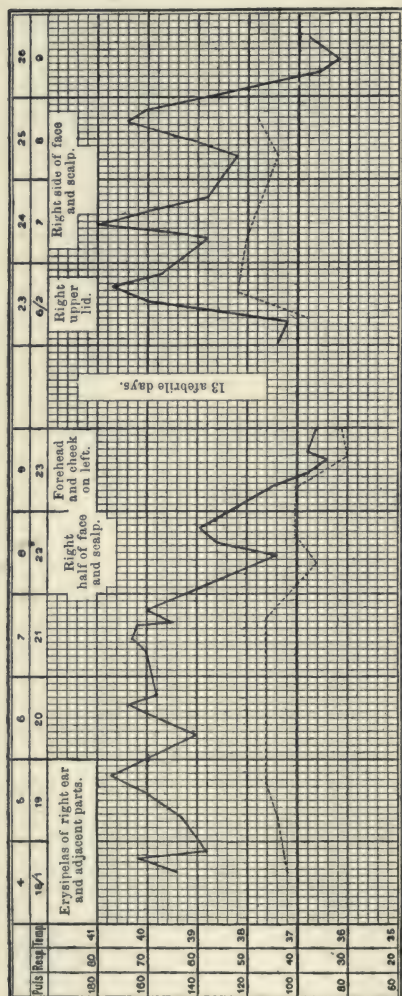
Fig. 33.

D., aged ten, was attacked, three days before admission, with violent pains in the neck and right ear. On the fourth day of the disease he exhibited, in addition to active redness and swelling of the elongated uvula (erysipelas of the mucous membrane?), a typical erysipelas of the right auricle and its

Finally, we would again recall the often quoted experimental inoculations of R. Koch and Petruschky,[33] who were able to produce a return of the erysipelas 11 times within two and a half months.

Relapses are in general far rarer than recurrences. Of our 140 patients, 7 (5%) had relapses, while the clinical histories of 27 (18.2%) revealed one or more previous attacks of erysipelas. Roger's[40] cases show 10% of relapses and 27% of recurrences. Among 89 patients, von Leyden and Renvers[64] observed 5 relapses and 19 recurrences. In Frickhinger's 528 cases there were 208 recurrences; of these, 116 had two, and 92 had three or more attacks.

The tendency to recurrences (in the restricted sense) is very variable. It is sometimes so pronounced that the designation "habitual erysipelas" is justified. In the great majority of these cases the face and scalp are affected, with the leg next in frequency. Chronic catarrh of the nasal mucous membrane and of the lacrimal passages, and chronic ulcer of the leg, especially when upon a varicose base, favor the return of the erysipelas, which develops in many individuals once or twice yearly, showing a special preference for the spring and autumn months. Women are affected three or four times as often as men. The development of the erysipelas is often favored in such individuals by picking the nose or scratching the leg, and in this manner producing superficial cracks in the tissues. If this cause is carefully considered, the return of such attacks of habitual erysipelas may often be prevented. From the frequent repetitions of the disease, the skin is often thickened, and sometimes to such a degree that cutaneous changes appear similar to those seen in elephantiasis. These have repeatedly been observed on the legs, in the scrotum, and on the vulva. They occur more rarely on the face, though unsightly deformities may also be produced in this situation.

Lambros (according to Friedrich[65]) records the case of a girl of twenty-one who had repeated attacks of erysipelas affecting the face, scalp, and right arm, between her tenth and thirteenth years. After the fifth or sixth attack she developed a great swelling of the face, the nose became thickened and seemed blunter, and the bridge and alæ were broadened. The eyelids, especially the lower, were transformed into heavy transparent, wrinkled sacs, and resembled alabaster. The skin of the forehead was so thickened that it could not be thrown into folds. The chief thickening was about the space between the eyebrows, and extended to both cheeks. The lips were swollen. The thickened parts were tense to the touch and did not pit on pressure.

Kaposi (according to Friedrich) repeatedly observed monstrous thickening and enlargement of the auricle and indurated swellings of the cheeks and lips after chronic recurrent erysipelas.

E. P. Friedrich[65] has described three similar cases from the Medical Policlinic in Leipzig. All were youthful individuals between the twelfth and seventeenth year. Two of these patients had had numerous attacks of erysipelas, which frequently recurred every month and lasted for ten days or two weeks. The swelling at the root of the nose, of the lids, cheeks, and lips was considerable. The skin was tense to the touch and did not pit on pressure.

In these fortunately rare cases it is highly probable that there is either a deficient absorption of the inflammatory exudate in the lymph spaces, or that an obstruction exists in the lymphatic paths, in the neighborhood of lymphatic glands, which causes the development of the lymphatic edema. This edema is differentiated from the edema of passive congestion by the fact that the affected portions feel harder and denser and do not pit upon pressure (Virchow).

In such cases it is quite possible, although not yet proved (see page 445), that bacteria remain in the inflammatory exudate and repeatedly rekindle the erysipelatous inflammation. These chronic cases are especially adapted to the investigation of these important questions. A small piece of skin could be very easily excised, sections cut and studied, and cultures made.

At all events, it is not unlikely that the chronic lymphangitis more or less retards the extension of subsequent recurrences, and consequently diminishes their duration and violence.

As a matter of fact, such a state of things is frequently observed. Many individuals affected with habitual erysipelas simply keep in their beds or in their rooms for several days and watch their "old comrade" disappear. This carelessness is readily understood when we remember that some individuals have passed through 5, 10, and 15 attacks of erysipelas. Thirteen of Roger's patients had from 5 to 7 attacks, five had from 10 to 13 recurrences, and two had had erysipelas 40 times. I do not possess such exact observations upon this point in our own series of cases, but the statement that several attacks of erysipelas have occurred is met with repeatedly. Youthful individuals may suffer from habitual erysipelas to such an extent that they are rendered unfit for military duty. The "Sanitary Report"[66] for 1895 states that a soldier was discharged at Ulm who had had erysipelas 20 times in the immediately preceding years, and mentions another who

was attacked by an erysipelas of the face and scalp 5 times before, and 5 times after, entering the service.

As before stated, the erysipelatous recurrences, and especially those of the habitual form, are usually milder than the first attack. Roger carefully examined 114 patients upon this point especially, and found the first attack to have been more violent in 69, and the second in 27.

It is nevertheless wrong to suppose that this will be so in a given case, for almost every experienced physician has made the sad observation that cases of habitual erysipelas may occasionally die in a recurrence, either as a result of general infection or of one of the previously mentioned complications.

4. ERYSIPELAS OF SUCKLINGS AND CHILDREN.

1. ERYSIPELAS OF THE NEWBORN.

This dreaded and almost uniformly fatal disease was formerly much more prevalent than at the present day. This is undoubtedly due to the fact that puerperal fever, especially in epidemic form, has become extraordinarily rare as compared with former times, and the newborn contract erysipelas not only from erysipelatous patients, but also from those with puerperal disease. Trousseau and Lorain[4] certainly laid the foundation for the recognition of the dependence of erysipelas neonatorum and kindred affections upon puerperal disease of the mother. Lorain observed that 50 out of 193 children viable at birth died from affections which strikingly resembled the fatal diseases of the respective puerperal women. The diseases most frequently coming under his observation were erysipelas and septic peritonitis or pyemia.

Both these sagacious observers pointed out that the physiologic wound at the navel of the newborn could be infected by the same virus that attacked the physiologic intra-uterine wound of the mother, and designated the erysipelas of the newborn as "puerperal erysipelas with the entire malignancy of the puerperal disease." We see that Trousseau, with the prophetic vision of a gifted investigator, clearly recognized a fact that has been confirmed by exact bacteriologic examination. There can be no doubt that the erysipelas of the newborn very frequently possesses a causal relation with puerperal disease of the mother, or of other recently delivered women in the neighborhood, and that it may be more frequent during endemics and epidemics of puerperal fever.

Bouchut[66] has also expressed a similar opinion. This form is certainly unusually dangerous, and the prognosis corresponds accurately with that of puerperal sepsis. The susceptibility of the newborn for erysipelas is fortunately not always present, since they may escape the infection even when they remain near the mother who has erysipelas or puerperal fever. They may also be spared when they have been born one or more days after the outbreak of the maternal erysipelas.

In these cases the erysipelas begins at the navel, at the vulva, or on the buttocks, and frequently first manifests itself by only a redness and tense swelling of the parts. On the following day the inflammation extends some centimeters and the characteristic sharply defined border may usually be recognized. Up to this point the child is only restless and fretful, but now, as a rule, the health visibly deteriorates and fever develops. Frequent vomiting and diarrhea follow, and as the erysipelas spreads over the entire body, the general loss of strength is so rapid that death frequently ensues upon the fifth, sixth, or seventh day of the disease. In spite of a pronounced wandering type, it is very rare for the disease to last more than two or three weeks.

The rash in general does not differ from that of the erysipelas of adults. The affected skin, however, often seems to be more tensely swollen, so that it becomes immovable, and the hands and feet are more frequently attacked than in adults. Areas previously affected are again involved by the disease. After the rash pales there often remains a more or less distinct edema. The occurrence of necrosis of the skin is much more frequent than in adults, and is observed especially in the scrotum and on the ankle, though it is also seen upon the back and the pinna of the ear. Abscesses are also relatively frequent, and according to many authors, Trousseau among them, their development is said to have a beneficial influence upon the general character of the disease. The French clinician quotes as an example the case of a child twenty days old, who recovered in spite of an extensive erysipelas, after an abscess had formed upon the back of the hand. Such a favorable termination must always be regarded as a rare exception to the rule that children in the first month practically always succumb to the disease. The severe infection is usually the cause of death, although abscesses, cutaneous gangrene, severe gastro-intestinal catarrhs, catarrhal inflammations of the lungs, and, above all, peritonitis also come under observation.

The erysipelas may, of course, proceed from other parts than those

already named. Vaccination sites and circumcision wounds are to be especially considered. In the latter case Henoch[67] saw the erysipelas proceed from the penis and wander over the entire body. After fourteen days there was a circumscribed gangrene of the scrotum, followed by a colossal abscess of the back, and death finally ensued from general collapse, icterus, and peritonitis.

The body-temperature usually varies between 39.0° and 40.5° and 41.0° C. (102.2° and 104.9° and 105.8° F.); the pulse is rapid from the beginning, 180 and over; the respiration varies between 60 and 80.

2. ERYSIPELAS OF SUCKLINGS AND OF OLDER CHILDREN.

After the second month the danger to the life of children attacked by erysipelas gradually decreases. Puerperal disease in the mother is naturally not so common a cause, but the disease originates in vaccination sites, in abrasions of the genitals and anus, in the frequent excoriations of scrofula, and in the eczema of the scalp which is so common in the first years of life. The last point of origin deserves special consideration, since an erysipelas concealed under the crusts and hair may not be seen until it appears on the forehead or neck, and the explanation of the pre-existing fever would be wanting until this time.

Scrofulous rhagades are a favorite point of origin for facial erysipelas, and they may give rise to frequent recurrences. This is worthy of careful consideration from a therapeutic standpoint, especially since a physician so experienced in children's diseases as Henoch emphasizes the fact that "nothing is more frequent than an erysipelas occurring once or even several times every year in scrofulous children with chronic rhinitis whose nostrils are excoriated and covered with crusts." I myself have not yet seen a "habitual" erysipelas in children, and I wish to quote a sentence written thirty years ago by Barthez and Rilliet[68] (page 41): "Is it not strange that just at the age when chronic inflammations of the face and scalp are so common, erysipelas is such an infrequent disease and so rarely complicated by cerebral symptoms?"

In my opinion, many local inflammations in children, such as are frequently seen about the nose in chronic scrofulous rhinitis, are incorrectly diagnosticated as habitual erysipelas. If the child has really had erysipelas once or twice, these inflammations are misinterpreted by the parents as repetitions of the disease, and so arises the statement that erysipelas has frequently recurred several times a year.

ERYSIPELAS AS A COMPLICATION OR SEQUEL OF OTHER DISEASES.

1. ERYSIPELAS IN CHRONIC DISEASES.

Erysipelas is the cause of death in many chronic diseases. This is especially true of bed-ridden hospital or private patients, who easily acquire an erysipelas, which leads to a fatal termination either by its extent or relative intensity. The character of the exanthem, the manner of its extension, and other concomitant symptoms may correspond in every respect to the typical picture of erysipelas.

Sometimes, however, sundry deviations are observed in reference to these points. The redness may occasionally be slight, the border not sharply defined throughout, and the fever slight or very irregular (asthenic form). A tendency may exist to punctiform hemorrhages or ecchymoses which are so arranged that they resemble acne rosacea (Juhel-Renoy et Bolognesi[69]), or gangrene may be unusually early in its development. This more malignant termination is particularly observed when the erysipelas proceeds from a bedsore where an opportunity for mixed infection has been given. Gangrene and a rapidly fatal termination may also occur in such a case, without infection by other bacteria. Such was the case in a woman of sixty-seven who came to us with an old and a more recent apoplexy. Death occurred upon the fifth day from an erysipelas of the trunk which had started in a bedsore over the sacrum. The streptococcus in pure culture was obtained from the blood and from the spleen.

Patients with cardiac and renal disease are particularly endangered when marked changes have occurred in the cardiac muscle. In our autopsy reports I frequently found the statement that the musculature of the right ventricle had been infiltrated with fat. Nevertheless, we not rarely see a good recovery, even in patients with cardiac disease, if the proper precautions are observed.

Juhel-Renoy[69] observed the "petechial type" particularly in alcoholics or in such men as had disease of the liver, heart, and kidneys.

Patients with chronic tuberculosis of the lungs are sometimes very unfavorably influenced by erysipelas. A particular tendency to hemoptysis has been repeatedly observed.

Individuals with chronic liver disease are greatly endangered, especially as they often have weak hearts and a tendency to delirium tremens. We observed this six times in our 140 cases, twice with a fatal result.

2. ERYSIPELAS IN ACUTE DISEASES.

Typhoid fever deserves first mention among acute diseases the course and convalescence of which may be disturbed by erysipelas. It is complicated by erysipelas much more frequently than is typhus or relapsing fever, and this is chiefly due to the varying durations of the three diseases. As a rule, the erysipelas does not associate itself with the typhoid fever until late in the disease, when bedsore and incised abscesses of the skin and of the parotid gland offer a point of entrance for the streptococci.

The frequency of this secondary erysipelas varies greatly; Louis saw it in 9 out of 134 cases, Chomel in 4 out of 42 cases, and Jenner in 7 out of 23 cases (see Murchison,[70] page 519). Not a few typhoid patients and convalescents die from this complication.

Diphtheria patients are usually endangered only when an external tracheotomy wound has been made. In other acute diseases erysipelas is seen, as a rule, only in those cases which are associated with bedsores and similar solutions of the continuity of the skin. I lost a strong man in the convalescence from a severe cerebrospinal meningitis from this cause.

RELATIONS BETWEEN ERYSIPELAS AND SCARLATINA.

The coincidence of scarlet fever and erysipelas is worthy of thorough consideration. I saw 4 such cases in less than two years, and will now give their histories, so that references may subsequently be made to them in the general consideration of this important question:

1. R., a girl, aged six, was admitted on the seventh day of the disease (July 18, 1895) in a very sick condition. A fading scarlatinal rash covered the entire body (the brother also had scarlatina at the same time), and a thoroughly characteristic erysipelas involved the left side of the neck and the whole anterior chest-wall, being accompanied by marked redness and an edematous swelling of the skin with a sharply defined irregular elevated border. The cervical lymphatic glands were markedly swollen on both sides, those on the left being united into an immense packet.

A discolored foul-smelling secretion flowed from the nose. The fauces showed a typical scarlatinal sore throat.

The temperature was 39.6° C. (103.3° F.), and during the following days varied between 38.8° and 39.6° C. (101.8° and 103.3° F.); the pulse-rate was about 160; the respirations were between 30 and 40. The lungs were clear and there was a palpable swelling of the spleen.

The erysipelas wandered, and, on the last day of life, involved the entire trunk anteriorly and posteriorly.

The autopsy showed a marked edema, but no purulent infiltration, of the skin of the anterior chest-wall. The cervical lymphatic glands were greatly swollen. There were necrosis of the soft palate, a soft swelling of

the spleen, and marked swelling of the mesenteric glands. Streptococci in pure cultures were obtained from the blood and from the spleen.

2. W. Martha, laborer's daughter, aged seven, was attacked seven days before, at the same time as her brother, with pains in the neck, a cutaneous eruption, and fever. Upon admission, March 18, 1897, the poorly developed child showed a moderate but sharply defined redness and swelling of the nose, a swelling of the tonsils which had a purulent coating, and a circumscribed necrosis at the end of the uvula. The cervical lymphatic glands were not actually swollen. The remaining skin showed neither exanthem nor desquamation. In the following days the erysipelas extended regularly but rather slowly until March 23d, when it reached to the ear upon the right side, and to beyond the pinna upon the right. Cessation of the disease and defervescence then ensued (Fig. 35).

Day of the Disease.
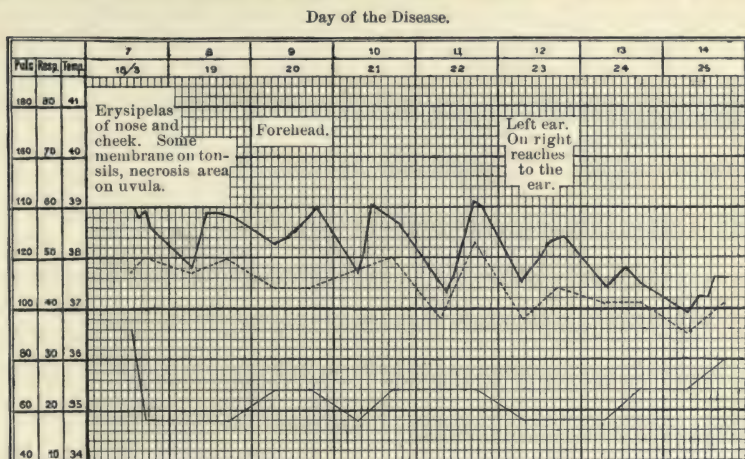
FIG. 35.

The injection of 10 c.c. of antistreptococcus serum from the Pasteur Institute had no effect whatever.

The third observation is of special interest, since the following affections were added to scarlet fever in the order named: croupous pneumonia, streptococcus empyema, erysipelas, and acute nephritis.

3. B., workman, aged twenty-six, was suddenly attacked, February 22, 1897, with violent pains in the head and limbs, vomiting, and diarrhea, and had an evening temperature of 39.7° C. (103.5° F.). During the next day a true scarlatinal rash developed which covered the entire body in the following twenty-four hours. Only a mild sore throat was present, but there was marked albuminuria. There was a continued fever (40.0° to 40.6° C.—104.0° F. to 105.1° F.) until February 25th, when it fell by lysis, reaching normal on February 28th, with a constant improvement of the general condition.

On the following day, however, the temperature rose rapidly to 40.2° C. (104.4° F.), with symptoms from the right ear. On March 3d turbid pus was removed by paracentesis. On March 5th a croupous pneumonia

(low down on the left, and posteriorly), followed with a characteristic sputum.   High remittent fever (temperature between 39.0° and 40.8° C. —102.2° and 105.6° F.).   The temperature fell by lysis, and was normal upon March 10th.   The pneumonia was undergoing resolution.

Other grave disturbances than ensued, which were indicated by numerous attacks of fever lasting from twenty to twenty-four hours, and sometimes reaching 41.3° C. (106.3° F.).   An effusion rapidly formed in the left pleural cavity and was removed by aspiration on account of the grave general condition.   It was seropurulent and contained streptococci alone. The fever was only moderate, but the general condition became worse daily.   The effusion quickly reaccumulated.

On March 24th an erysipelas began on the nose, and continuously advanced until March 27th, remaining limited to the face.

On March 26th, 1500 c.c. of a thin pus were removed from the chest; on March 28th, after a resection of the ribs, 1200 c.c. were obtained, yet death ensued nine hours later.

The albuminuria was often very great, reaching 8% (Esbach), although the microscope failed to reveal a corresponding increase of the morphologic elements.

At the autopsy a large quantity of thin pus containing streptococci was found in the left pleural cavity.   The pleura itself was covered with thick fibrinous coagula.   The left lower lobe was collapsed; the lower portion of the right lower lobe was in the stage of red hepatization; the lungs elsewhere were crepitant.   The heart was flabby and its muscle cloudy; the valves, the endocardium, and the pericardium were normal. The spleen was large, soft, and brownish-red; its cut surface bulged and could easily be scraped off.   The liver was slightly cloudy.   The kidneys were large and their capsules peeled off easily.   On section, the entire organ was cloudy, the cortex was markedly prominent and pale.   The brain showed no pathologic changes.   Streptococci in pure culture were obtained from the blood and from the spleen.

4. Helene O., girl, aged twenty-three, was admitted in January, 1898, with typical scarlet fever.   On the fourth day of the disease, when the temperature was only 38.4° C. (101.1° F.), the erysipelas began upon the nose.   During the following days it extended over the right cheek.   After the disease had practically ceased and desquamation had appeared a relapse of the erysipelas occurred, which again started from the nose and extended over both cheeks and upon the forehead as far as the roots of the hair.   The patient had suffered from several previous attacks of erysipelas.

We have already touched upon the question as to whether intimate relations existed between erysipelas and scarlet fever (page 437), but we must now carefully consider the subject, since Babes,[71] Brunner,[72] and others have ascribed scarlet fever to a "modified streptococcus infection."   At the very outset, it cannot be denied that a series of weighty clinical objections contradict any such theory.   Disregarding the fact that erysipelas shows a great tendency to recur, while scarlet fever usually attacks the individual but once, we might point out that the coincidence of the two diseases is very rare, and does not bear comparison with the simultaneous appearance of puerperal fever and

erysipelas, so commonly observed formerly. On the other hand, we must admit that in a careful collection of all known cases of surgical scarlet fever, C. Brunner quotes authors who have observed both diseases side by side. I would also mention an article of my brother's, S. Lenhartz,[73] in which he points out that Professor Heubner contracted a typical facial erysipelas while treating a case of severe scarlatinal sore throat. A series of observations of special interest are those of Rocochon,[74] who saw the following diseases hold causal relations:

1. A man had a varicose ulcer of the leg which led to lymphangitis and a general scarlatinal exanthem.

2. A woman who visited this man was attacked by facial erysipelas. She had never had the disease previously.

3. The husband of the former was attacked by an acute suppuration of the axillary glands, no other definite cause being found.

4. A few days later a recently delivered woman "in the same village" developed typical scarlatina.

5. A young man who visited the first patients was likewise attacked by facial erysipelas.

It is far from our intention to infer that an absolute dependence existed between these cases observed simultaneously and successively. When we recall the relations existing between puerperal fever and erysipelas, however, and when we hear from such experienced obstetricians as Braxton-Hicks[75] and Playfair[76] that puerperal women who had come in contact with scarlet fever were attacked by puerperal fever, and that they saw scarlatina transmitted from the puerperal fever, the hypothesis gains color that erysipelas, puerperal fever, and scarlatina are caused by similar bacteria, and that the special conditions under which they develop, singly or together, are as yet unknown.

One point out of many others always reawakens our objections, and that is the fact that the demonstration of streptococci in uncomplicated cases of scarlatina has seldom (Babes) been successful. To this extent we consider the objections expressed by Jürgensen[20] and Baumgarten[77] as very appropriate. Their conclusions are not sufficiently supported, however, when they infer from a fatal case of scarlet fever of but thirty-four hours' duration, in which streptococci could be found in no other organs but the tonsils, "that streptococci cannot be the exciting cause of scarlet fever, if scarlet fever appears fully developed without streptococci." We would only point out that, even in puerperal sepsis, the most careful bacteriologic investigations are sometimes negative, and that all the culture-media inoculated remain

sterile, although the clinical observation, the fatal termination, and the results of the autopsy leave no doubt as to the correctness of the diagnosis. Their case stands alone, inasmuch as the bacteriologic examination of a similar case has not yet been reported.

It follows from all this, that further proof of relations between these three diseases must be diligently sought for. Careful observations should be reported in the future, and probably more definite relations may become apparent in a larger number of cases.

For the present, the idea seems to me to be still better founded which ascribes to the streptococcus a secondary rôle in scarlatina as an exciting cause of the complications; that is to say, of the secondary infections. At all events, there is no doubt that we meet with streptococci in all cases of septic scarlatina. In our previously mentioned cases in which scarlatina and erysipelas occurred simultaneously, we found these parasites in pure culture in the cadaveric heart's blood and in the spleen.

DIAGNOSIS.

As a rule, the diagnosis of cutaneous erysipelas is easy and certain when the exanthem has extended over an area about the size of half a dollar [or two-shilling piece]. A solution of continuity of the skin is not rarely found as a point of origin. In addition to the bright glistening redness and the distinct swelling, the border is specially characteristic. If this is linear, more or less irregular, but sharply marked off from the healthy skin, the erysipelatous character of the inflammation is not to be doubted. In the differentiation of a phlegmon or of a lymphangitis from an erysipelas, great stress is to be laid upon this characteristic. Other distinctions may usually be observed: in phlegmonous inflammations the redness is darker and the swelling is firmer, as hard as a board, from the involvement of the deeper tissues; in lymphangitis, there are present distinct hard cords, corresponding to the lymphatic vessels, or red areas connected with each other, instead of the homogeneous diffuse redness of erysipelas. As previously stated, erysipelas is also characterized by the formation of numerous vesicles of varying size upon the reddened skin. In phlegmon and in lymphangitis these are absent and the tendency to suppuration is very great.

In rare cases malignant pustule upon the nose (or behind the ear) may give ries to confusion. Palpation will generally prevent an error of diagnosis, since the swelling of anthrax is very firm and is characterized by the central depressed scar. The microscope and the inoculation of culture-media will immediately confirm the diagnosis.

Other inflammatory cutaneous eruptions rarely come under consideration from a diagnostic point of view. Erythemata are usually more fleeting, and differ from erysipelas in their rapid general extension and the absence of pain. Erythema nodosum, the individual eruptions of which are actively red, swollen, and painful, appears in such numerous scattered areas over the extremities and the entire body that any confusion with erysipelas is out of the question. This is also usually the case in urticaria.

I once saw a peculiar exudative erythema in combination with a scarlatinal rash. In addition to the general, well-characterized, diffuse redness, composed of bright red dots, there could be perceived in the

first five days of the disease symmetrically situated, actively reddened, and tensely swollen areas, which were difficult to differentiate from an erysipelas, because the swollen areas were sharply outlined from the surrounding dotted region. Such eruptions occurred successively upon the cheeks, arms, and legs, and were accompanied by continuous fever. (Appropriate culture-media were inoculated with the blood, but they remained sterile.)

An actual erysipelas occurring with scarlatina, such as we have described on page 494, was excluded chiefly because the rapidly advancing cutaneous swellings were observed simultaneously upon the face, arms, and legs, and there was no demonstrable connection between these large areas of cutaneous redness. It is therefore most likely that an exudative erythema was present in addition to the scarlatina. On the other hand, it is also possible that it was only a severe case of scarlet fever in which the toxins not only produced a continued fever and prostration for almost sixteen days, but also the peculiar violent irritation of the skin.

The differentiation from zoonotic erysipeloid is of practical importance. This exanthem, first described by F. J. Rosenbach,[78] and which will be specially considered at the close of this monograph, may actually be confounded with true erysipelas. This error will be always avoided if the description of the disease is carefully considered. In all afebrile exanthemata of the face which extend over one or both cheeks, —generally like the wings of a butterfly,—the first thought should be of erysipeloid. I do not doubt that this affection has frequently given rise to the supposition of an afebrile erysipelas. I have several times had the opportunity of correcting such diagnoses, and consequently recommend attention to this point.

The diagnosis of erysipelas of the mucous membranes is much more difficult. With rare exceptions (see Laryngeal Erysipelas, p. 466) it is to be certainly diagnosticated only when preceded or followed by a cutaneous erysipelas. Redness and swelling are by no means characteristic; the concomitant phenomena—glandular swelling, fever, albuminuria, swelling of the spleen—may appear in any active inflammation of the throat. It is always well to think of erysipelas, however, in those cases of sore throat which commence acutely with a chill, and proceed with active redness, swelling, painful enlargements of the lymphatic glands, and marked constitutional symptoms. [In the editor's experience, the erysipelatous sore throat is remarkable for the intense pain which accompanies it.]

We will take this opportunity to also consider those very malignant

pharyngeal disturbances to which Senator first directed attention—
the acute phlegmonous infection of the pharynx.

When Senator[79] reported his first observations to the Berlin Medical Society, in 1888, their significance was actively called in question by
P. Guttmann,[80] with whom Virchow also agreed to a certain extent.
Senator reported the cases of two men, aged twenty-nine and thirty,
who were suddenly attacked with a chill, gastric disturbances, and
dysphagia, and died upon the fifth and eighth day of the disease respectively. They had had, in addition to delirium and marked constitutional symptoms, an active redness of the pharynx, with no
specially marked swelling, but with great tenderness to external pressure, and died from rapid loss of strength without signs of suffocation.

At the autopsy a purulent phlegmon of the pharynx was found with
involvement of the tonsils and of the larynx, the spleen was enlarged
and crumbled under light pressure, and there was a parenchymatous
nephritis.

We fully agreed with Senator, who regarded this condition as something peculiar to itself, something that could appear without erysipelas. It should not be said, however, that a similar clinical and pathologic condition cannot appear in the train of an erysipelas. On the
contrary, we emphasize this possibility, since we have learned to recognize the secondary appearance of phlegmon in cutaneous erysipelas as
the effect of the same coccus which had previously caused true erysipelas in the same individual.

In the discussion at that time, Virchow[81] reported the following
personal observation:

A recently delivered woman was attacked by severe puerperal fever
with local uterine phenomena. Her little boy soon afterward contracted
an erysipelas which became gangrenous. Swelling of the scrotum. Cyanosis. Death in an attack of suffocation.

The autopsy revealed an acute infectious phlegmon of the pharynx.

PATHOLOGIC ANATOMY.

THE exanthem upon the dead body is in general only slightly characteristic; the sharp elevated border is entirely absent. The flabby enlargement of the spleen, such as we find in most acute infectious diseases, is one of the most constant demonstrable changes.
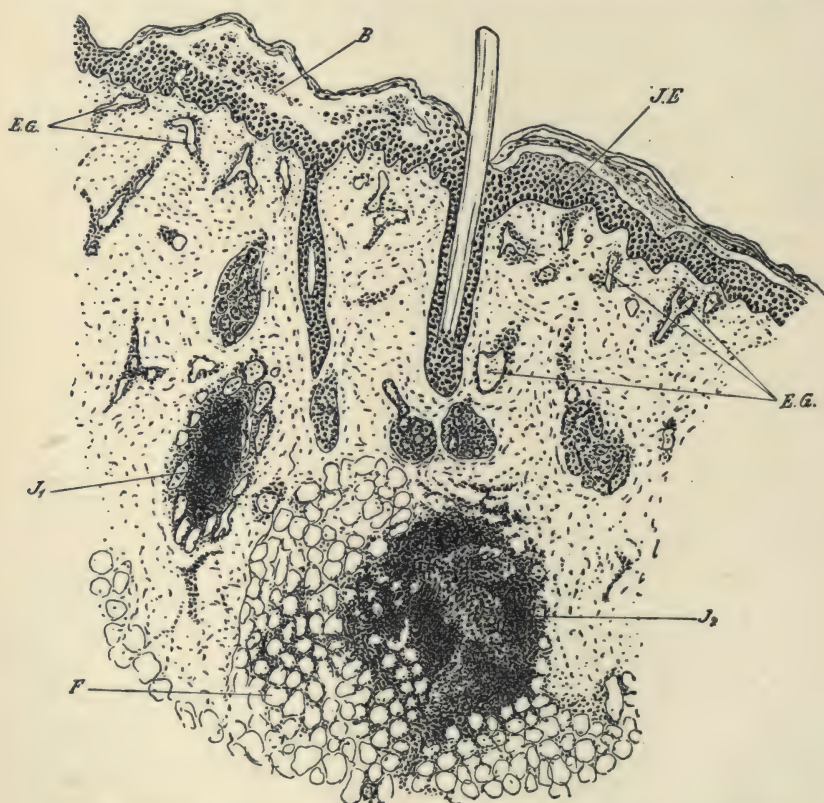
FIG. 36.—General view under the low power; section through an erysipelatous area of the skin: *B*, Vesicle; *JE*, inflammatory infiltrate in the epithelial layer of the skin; *EG*, dilated vessels; J_1 and J_2, collections of bacteria; *F*, fatty tissue.

Parenchymatous changes in the heart, liver, and kidneys are not rarely present, and their exact description has already been given in the various autopsy reports. The consideration of the grave tissue changes found in gangrene, phlegmon, and purulent edema, and in

the general sepsis that may follow in the train of erysipelas, will be taken up under the septic diseases.

We will now more carefully consider the microscopic changes which may be observed in pieces of skin removed from erysipelatous areas in the dead, or, still better, in the living (Figs. 36 and 37).

It has been certainly established by Volkmann and Steudener[82] and others that in erysipelas there is not only hyperemia and edematous infiltration of the skin, but also a more or less dense round-cell infiltration in the cutis and subcutaneous tissue. Sometimes these inflammatory changes are chiefly in the deeper layers of the cuticle, and sometimes all the layers are equally affected. In one case the
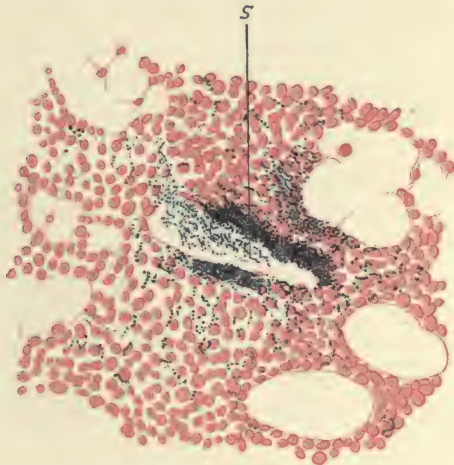
FIG. 37.—The same section with the area J_1 under a high power. Zeiss 1 ; oil immersion, $\frac{1}{12}$. *S*, Collection of streptococci.

changes in the skin preponderate, and in the other they are more marked in the subcutaneous areolar tissue. At the height of the disease the tissues are more or less markedly swollen and the fibers of the cutis are separated by the exudation, so that the skin as a whole seems considerably thickened. The vessels of the cutis are markedly dilated and numerous migrated leucocytes are often seen in layers in the perivascular tissues. A small-cell infiltration frequently conceals the vessels in the corium, and a dense accumulation of round cells may be seen between the groups of fat cells of the subcutaneous tissue. Where retrogression is indicated by the decreasing redness and swelling of the skin, the round-cell infiltration has almost entirely disappeared. This takes place partly by granular

degeneration and partly by absorption, as is shown by the densely packed lymphatic vessels in these districts. The skin often appears entirely normal upon the fourth day, in contrast to phlegmon and pseudo-erysipelas, in which purulent liquefaction and necrosis of the tissues take place. If the infiltration is unusually massive, gangrene may occur in certain situations which have been previously indicated. An examination of the vesicles shows that the cells of the rete Malpighii are swollen and the uppermost epithelial layers (stratum corneum) are elevated in areas of varying extent. The cavities formed in this way are filled with an exudate rich in cells. The migration of the leucocytes from the papillæ to the layers of epithelium may often be distinctly followed. The two illustrations (Figs. 36 and 37) exemplify these changes better than any description of the condition. The epithelium of the sebaceous glands and hair follicles also shows certain changes. The hair follicle may be separated from the root sheath by a serous exudate, so that the hair is elevated from the papilla, thus explaining the baldness so frequently seen in erysipelas. At the height of the disease the more exact investigation of stained sections shows that the sharp border of the erysipelatous area may be differentiated into three zones: The peripheral zone, macroscopically unchanged, shows numerous micrococci in the lymph spaces; the middle zone, corresponding to the raised inflammatory edge, is characterized by the massive round-cell infiltration and lymph spaces densely packed with cocci which are partly intracellular; in the third zone we shall find some round-cell infiltration, but no cocci.

PROGNOSIS AND MORTALITY.

Ordinary uncomplicated erysipelas may be generally regarded as a thoroughly benign disease. The prognosis becomes materially worse if the erysipelas occurs as a secondary disease, if it attacks the larynx primarily, or if it appears upon the genitals of a puerperal woman. Great danger is also added if the disease extends over the entire body (erysipelas migrans), since the general strength of the patient often suffers severely. The fact has already been emphasized that newborn children attacked by erysipelas in the first month almost always die. Trousseau regarded the erysipelas of the newborn as uniformly fatal; Steiner lost 58 children out of 60 cases.

It is also worthy of special mention that even uncomplicated erysipelas may terminate in death as a result of the severe infection, the autopsy revealing no other explanation for this termination. Even youthful individuals may be sacrificed by this disease. On the other hand, in addition to the previously described complications, death may be caused by sepsis, due to the passage of the streptococci into the circulation and their further multiplication. This series of events is fortunately quite rare. Two such cases have been detailed on pages 479, 480. In the following section upon the septic diseases we shall come back to this point.

It is evident that chronic alcoholism has an extremely unfavorable influence upon the prognosis.

The calculation of an average mortality is of no practical value. From 10,000 cases of different authors (surgical authors included) collected by Zuelzer,[15] he calculated a mortality of 11%. Blass, according to Zuelzer (Medical Clinic at Leipzig), found a mortality of 3%, Volkmann[5] (Halle) 5%, Ritzman (Berlin) 7.8%, Heyfelder[15] (Petersburg) 10%. Roger gives a mortality of 4.53%. In the "Sanitary Report of the Royal Prussian Army" from 1884 to 1888 there are 4115 cases of erysipelas, with 35 deaths; i. e., 0.85% mortality, a figure which bears eloquent witness to the quality of the material, to the excellent medical service, and to the hygienic conditions of these hospitals.

[One of the aphorisms of Hippocrates on erysipelas is well worth quoting. It runs thus: "'Ερυσίπελας ἔξωθεν καταχεόμενον εἴσω τρέπεσθαι οὐκ

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ἀγαθόν, ἔσωθεν δὲ ἔξω ἀγαθόν": " For superficial erysipelas to turn inward is not a good sign; for internal erysipelas to become superficial is a good sign."*]

Hippocratis Coi Aphorism, Lib. vi, Sec. 7, Aphor 25.   Editio Foesii, Francofurti, 1624.

PROPHYLAXIS.

THERE is undoubtedly a large field for prophylactic measures. The history of the last decade has taught that the number of cases of erysipelas has diminished, particularly in hospitals, with the growing understanding of antisepsis and asepsis. The danger of transmitting erysipelas to injured or operation cases has become less from year to year. In 1886 Küster[43] published a very clear review of this happy state of affairs. In his surgical wards at the Augusta Hospital in Berlin the percentage of erysipelatous cases in the years 1871–1885 sank from about 7% to 0.74%. The chief decrease began with the introduction of the antiseptic treatment of wounds.

Since we have come to know the cause of the disease with certainty, this and similar experiences do not seem strange to us; we even regard them as self-evident, and strive to protect the injured and operation cases from erysipelatous patients. We consequently regard the rigid isolation of erysipelas from surgical wards as an urgent necessity. In no less decided terms must surgeons be warned against performing any operation if they have fingers affected with a commencing or a fading erysipelas.

It is questionable whether it is as necessary to isolate erysipelas patients from medical wards. The particular group of diseases with which they may come in contact must be considered. It is self-evident that typhoid and other patients having bedsores and pre-disposed to erysipelas must be protected from contact with the disease. If this precaution is observed, and the case is otherwise carefully treated, the immediate transmission of the disease will be extremely rare, as I can testify after a hospital experience of many years. On the other hand, I wish to state that many clinicians believe also in the isolation of medical erysipelas. Gerhard[83] is one of these, since he saw an orderly who had nursed an erysipelatous patient attacked by a right-sided sore throat. The day after the disappearance of the exudate a facial erysipelas developed which had extended to the right cheek through the right side of the nose.

We are by no means secure from the introduction of the disease from without. Many patients having wounds or suppurations carry

the germ with them before the erysipelas distinctly appears. The disease is consequently introduced into the most modern hospitals, and gives rise to no small number of cases of erysipelas. Not a few cases of erysipelas are admitted to medical wards with symptoms of nothing but a simple sore throat, and the erysipelatous character of the disease is not apparent. The disease does not appear upon the skin for one or more days, and then the condition of affairs is plain enough. In these cases transmission is as difficult to avoid as in those cases of scarlatina in which the eruption does not appear until the third or fourth day of the disease, the only symptoms present being those of afebrile sore throat.

To avoid the transmission of both infections I have, for some time, regularly isolated the sore throats for several days if possible. The procedure is also of advantage in other respects.

From the detailed account of the intimate relations existing between erysipelas and child-bed fever, it follows that puerperal women are to be carefully guarded from the slightest contact with erysipelatous patients. The same caution must be observed with the newborn, for although the predisposition to erysipelas is not so very well marked, the danger to life from an attack of the disease could not be greater.

Great attention should be devoted to those disposed to "habitual erysipelas." Such persons very frequently suffer with chronic nasal catarrh and the formation of rhagades. They often have considerable itching, which they try to relieve by picking at the nose. In these cases the return of the erysipelas may often be permanently prevented by treatment of the nasal condition. In a number of elderly individuals (3 women among others) who suffered from repeated recurrences of facial erysipelas I have obtained good results by advising them to simply rub cold cream into the nostrils night and morning, working it into the nose by rubbing the alæ and simultaneously snuffing it up, so that it would be evenly distributed. The habitual erysipelas, which in some cases had recurred seven or eight times, troubled the patients no more, although they have been under my observation for over fifteen years.

TREATMENT.

IF we believe Trousseau's statement that "erysipelas belongs to the diseases which recover spontaneously," there is good reason for astonishment at the surprisingly large number of remedies that have been recommended for this disease. It would lead us too far and be of little value if we should describe all the methods of treatment, or even only those employed and esteemed in the last ten years. We deem it better to consider the chief points of view that have been held in the treatment of the disease and to clearly state our own opinion.

Disregarding the newest specific serum treatment, which will subsequently be fully considered, those local methods must first be mentioned the aim of which is to hinder the extension of the advancing erysipelas or to produce an arrest or the retrogression of the process. We try to attain this result by purely mechanical means, by chemical agents, or by a combination of these treatments.

1. REMEDIES EXERTING CHIEFLY A MECHANICAL INFLUENCE.

The procedure recommended by Wölfler[84] deserves first mention.

Wölfler placed strips of adhesive plaster at some distance from the erysipelatous border, arranging them in a circular manner if possible, and making great tension, so as to hinder the further advance of the streptococci along the lymphatic paths. If this method is properly carried out, the erysipelas is said to halt at the strips of adhesive plaster. At this point a great swelling develops, which does not disappear for several days. Should it become threatening, local depletion should be performed by means of scarifications or leeches. Should a strip become loosened, it is advisable to apply a "safety strip" at some distance from the first one. The strips should not be removed until from four to eight days after the fall of the temperature. In 1891 Wölfler reported over 60 cases in which he had obtained very good results with this treatment. In every case of erysipelas of the head and face he saw the disease brought to a standstill. My own experience with this method, in the few cases in which I was able to carry it out, soon led me to give it up. Even in the arms, in spite of

early and marked constriction, I have seen the erysipelatous outposts slowly advance and creep under the adhesive strips. The method does no harm if it is carefully watched and the great swelling near the strips is not allowed to go on to necrosis. This may be prevented by scarifications at the proper time or by loosening the strips of plaster.

According to Kroell,[85] the disease may be arrested by an elastic bandage which is applied with moderate firmness. If the extension of a facial erysipelas to the scalp is to be prevented, the bandage must be carried about the head like a hoop and the region about the ears protected by layers of cotton. The results are said to be excellent. At all events, this method has advantages over that of Wölfler, since the degree of constriction may be changed at any moment and the discomfort attendant upon the removal of the plaster from hairy surfaces is avoided.

Instead of the constriction of adhesive plaster or bandages, P. Niehaus[86] and others have recommended the application of a circular strip of collodion as broad as the palm of the hand. A second ring may be painted above the first, analogous to the "safety strips" of Wölfler, so that the germs which slip past the first protective barrier may be arrested at the second.

These methods all aim at preventing the advance of the infectious germ in a purely mechanical way, and thus limit the disease to the locality. Other methods have been devised to directly inhibit the growth of the organism by keeping the air away from erysipelatous surfaces. Oil paint and varnish have been employed for this purpose. The method first recommended by Barwell has been followed by scarcely any one, although it should be mentioned that in the 5 cases in which he painted over the erysipelatous area the disease was very quickly arrested. Instead of oil paint, Otto[87] employed a solution of 2 parts wax and 20 parts "dryer" in 100 parts of linseed-oil varnish. In all of the eight cases in which he employed this procedure he observed a rapid fall of temperature and an arrest of the local phenomena within the next twelve or twenty-four hours.

According to Kolaczek,[88] the air may be excluded in the following simple manner: The entire erysipelatous area and a hand's breadth of the healthy skin is smoothly and firmly covered with rubber protective. In certain regions of the body, where the protective will not lie close to the skin, cotton and bandages must be applied. If the erysipelas advances, fresh protective is to be applied to a corresponding extent. Good results are said to be attained. It is uncertain whether chemical influences are at work in addition to the effect of the exclu-

sion of the air. At all events, the simplicity and the safety of the method invite further trial.

Good results have frequently been claimed from repeatedly painting the erysipelatous area and its neighborhood with collodion. The combination of collodion with ichthyol, however, has found a much more extensive use. This brings us to the consideration of those agents which have partly a mechanical and partly a chemical influence, and which have been especially esteemed in more recent years.

Ichthyol-collodion is employed in a strength of from 10% to 50%. It is painted in a tolerably thick layer, not only over the erysipelatous area, but also over the surrounding healthy skin for 2 or 3 centimeters ($\frac{4}{5}$ of an inch to $1\frac{1}{5}$ inches). Again, a mixture of ichthyol and vaselin in the proportion of 1 : 3 or 1 : 1 may be rubbed daily over a similar area. There is a marked difference of opinion concerning the influence exerted upon the inflammatory process by this remedy. While not a few report the most brilliant results, others have seen no effect whatever, and are by no means convinced of its specific curative action. Nussbaum[89] furnished the first reports of the effect of ichthyol upon erysipelas. He found a complete cessation of the disease upon the day following the inunction: "The rapidly swollen, glistening, succulent skin was quite sunken in and shrunken into brownish-yellow folds; the pain upon pressure which had existed the day before gave place to a sensation of formication—in a word, every symptom of irritation had disappeared as if by magic, and did not return, although the inunctions were made only three days in succession." Nussbaum referred this result to the reducing effect of the ichthyol, which so acted upon the tissues that the cocci could neither increase nor develop their pathogenic properties. This view of Nussbaum, at first founded upon a few cases, was supported particularly by Fessler,[90] who collected reports of 397 cases of erysipelas from the Munich Hospital, in which different therapeutic measures had been employed. In 53 cases which were treated with ichthyol exclusively he found the average duration of the disease considerably—about one-half—less than with other methods of treatment. Fessler, Klein,[91] and others advised that the ichthyol treatment should be continued until well on in the convalescence. The inunctions are to be repeated two or three times daily, previously washing the skin thoroughly with soap and water or salicylic acid solution. The salve is then to be rubbed in from the healthy neighboring districts toward the diseased area, a sufficient quantity being employed to color the skin a homogeneous dark

brown. The entire surface is then covered with moistened gauze and
cotton, which may be held in place by a loosely applied bandage.

It is questionable whether there is a direct bactericidal effect as well
as a reducing one; Fessler nevertheless points out that the develop-
ment of the streptococcus ceases if bouillon contains more ichthyol
than 1 : 4000.

From my own experience, the supposition of the strikingly favor-
able or specific influence of ichthyol in erysipelas has not been sup-
ported. On the contrary, in spite of the uniform employment of the
remedy I have observed not only a continuous advance of the disease
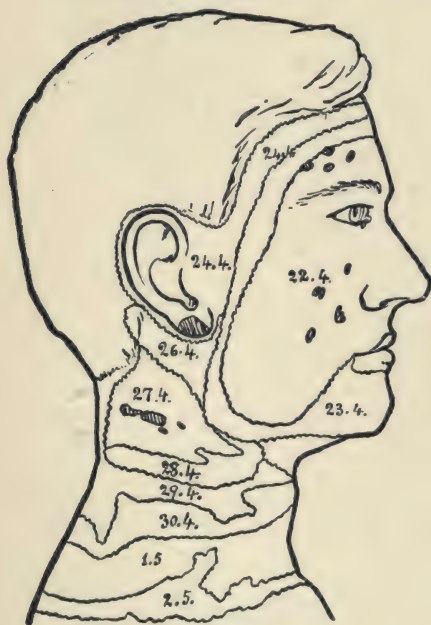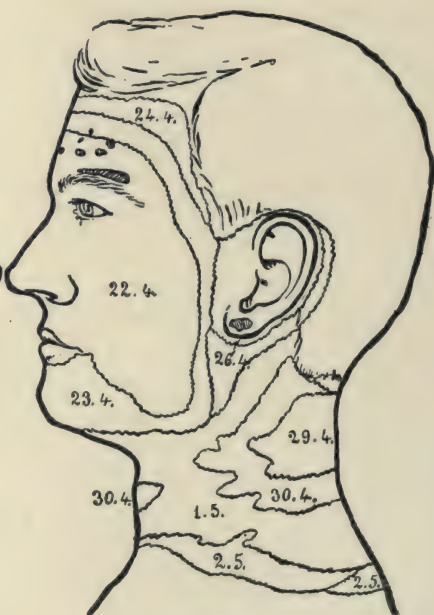
FIG. 38.   FIG. 39.

in erysipelas migrans, but also a fatal termination. This may be seen
from the following brief notes and sketches of cases, together with their
temperature curves:

1. L., servant, aged twenty-four, was attacked suddenly and for the
first time with a facial erysipelas which proceeded from the nose. On
admission, upon the fourth day of the disease (April 21, 1897), there were
severe constitutional symptoms without demonstrable complications.
The advance of the erysipelas is shown in figures 38 and 39; the accom-
panying chart (Fig. 40) shows the temperature curve. During the first
days the patient was treated with bichlorid applications, and from the
morning of April 26th with inunctions of 50% ichthyol ointment, repeated

several times daily. The erysipelas continued to advance until death
ensued from exhaustion, the autopsy revealing no other explanation.

2. Wilhelmine E., servant girl, aged twenty-two, was attacked November 15, 1897, with pains in the left ear. She had had a slight injury in
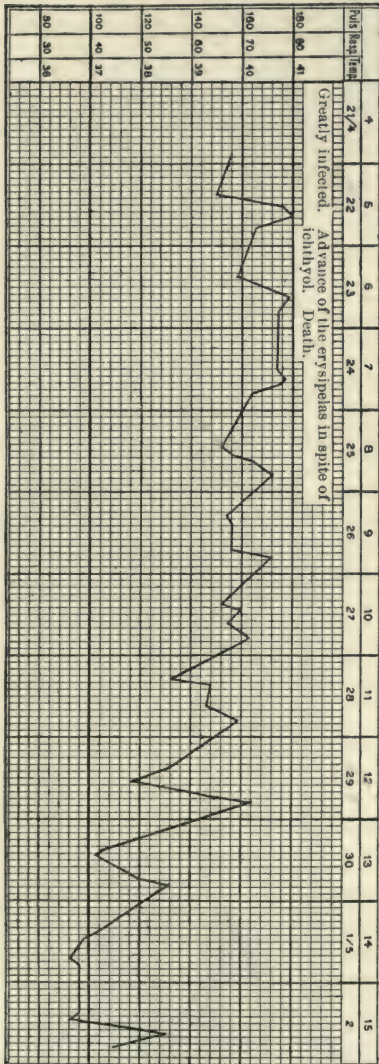
Fig. 40.
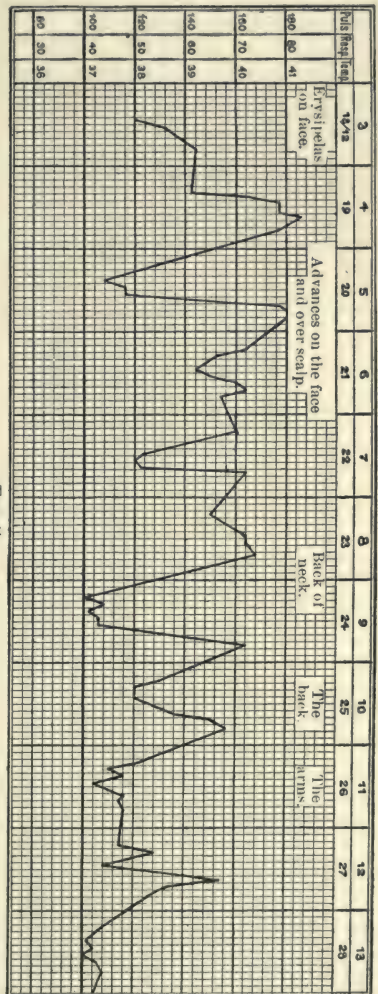
Fig. 41.

this situation, which had scabbed over. Chill on November 16th. First
attack of erysipelas, the disease involving the entire left half of the face.
The area was painted over with a thick layer of ichthyol-collodion, and
this treatment was continued. The erysipelas, however, rapidly advanced

over the scalp and to the right side of the face. On November 22d, the erysipelas had extended to the neck; a thick and broad strip of ichthyol-collodion was painted around the neck, extending 6 centimeters ($2\frac{1}{5}$ inches) beyond the erysipelatous border. As the disease had advanced far beyond this strip on November 23d, the painting was discontinued. The disease advanced over the back and arms until November 29th, when the outrunners were paler, more speckled, and not so painful. The axillary glands were swollen.

In addition to ichthyol, a number of external remedies are recommended, which can only be briefly mentioned.

Hamburger[92] claims to always arrest erysipelas, not rarely with a rapid fall of temperature, by paintings of tincture of iodin (once or twice daily) extending 2 or 3 centimeters beyond the erysipelatous border. Signs of irritation are said never to occur.

Koch[93] obtained a similar result after the application of a salve consisting of creolin 1 part, iodoform 4 parts, and lanolin 10 parts.

Amici[94] claims to obtain an abortive effect by painting the visibly inflamed areas, and those sensitive to pressure, every two hours with equal parts of carbolic acid and alcohol. In the case of tender skin also, equal parts of carbolic acid and glycerin, or a 1% solution of corrosive sublimate in glycerin, may be used. Many prefer sublimate with lanolin, 1 : 1000.

Sprays of bichlorid are also used. Cayet[95] and Talamon[96] saw the process arrested in twenty-four hours after sprayings of sublimate (two or three times daily, one minute each), and the average duration of the disease was decreased to four days. The spraying solution of Cayet has the following composition:

℞. Hydrargyri chlor. corros.
    Acid. citric...............................āā 1.0 (gr. xv)
    Alcohol absol............................... 5.0 (gr. lxxv)
    Æther sulph............................ q. s. ad 100.0 (℥ iij ʒ j).

Talamon recommends that the spray be followed by applications of boric water and 1% ethereal solutions of sublimate.

The only disagreeable secondary effect is said to be the appearance of small pustules or the increased formation of vesicles.

Schwimmer[97] recommends 30% to 50% solutions of resorcin in glycerin; Behrend[98] advises the energetic washing of the erysipelatous area three times daily with absolute alcohol; v. Langsdorff prefers to apply the alcohol by means of a thick layer of soft linen, covering this over with taffeta. Fever and swelling are said to disappear in twelve to twenty-four hours, and the parts are entirely normal in three to five days.

Lücke[99] saw excellent results from rectified spirit of turpentine. This should be rubbed in or painted upon the surface four or five times daily, always passing from the healthy toward the diseased skin. Mull is loosely applied over this and the procedure repeated in a few hours. In the beginning there is marked itching and burning which are said to soon disappear.

[Topical or local treatment has three ends in view: First, to relieve pain and tension; secondly, to check the spread of the inflammation; thirdly, to destroy the infectious matter *in situ*. The first indication is met by covering the affected part with cotton-wool so as to exclude the air; by dusting it over with a mixture of oxid of zinc and salicylated starch, or, better still (for, when wet, it does not cake on drying), with a mixture of oxid of zinc and lycopodium powder, of each half an ounce, intimately shaken up with 15 to 30 minims of liquefied pure carbolic acid. Marc Sée, of Paris,* employs subnitrate of bismuth as a dressing. It is a preventive as well as a curative agent. It should be dusted as a powder topically over the solution of continuity, which is the point of departure of the malady. Subgallate of bismuth (better known as "dermatol") is recommended as a powerful non-irritant antiseptic and desiccant, free from odor or poisonous properties. It is now official in the German Pharmacopœia and is found in the Addendum to the Austrian Pharmacopœia also.

If the foregoing means fail to give relief, the affected part should be fomented with flannels wrung out of a hot decoction of poppies, as long since recommended by Sir Thomas Watson, or covered with spongio-piline soaked in hot water and sprinkled with laudanum. The old-fashioned prejudice against "wetting the nose" has long since been given up—in medical circles at all events.]

In the methods mentioned up to the present the aim has been to spare the tissues as much as possible, inasmuch as bloody procedures have not been considered. In the following three methods they have been employed in a more or less reckless way:

Hüter[100] was the first to proceed in this energetic manner. Being convinced that bacteria were the cause of erysipelas, he advised the subcutaneous injection of a 2% carbolic solution, repeated once or twice daily. These injections were made at a short distance from the erysipelatous border, the needle being introduced through healthy skin and the injection made toward the diseased area. This procedure has been tried a great number of times, and while it has certainly helped many cases, it has been absolutely worthless in a still larger number.

* Paul Lefort: *La Pratique Journalière des Hôpitaux de Paris*, 1891, p. 153.

In addition, the method is painful, and consequently it was rightly discarded. At the same time, Küster similarly advised the injection of 1 : 1000 bichlorid solution; to-day scarcely any one would carry out the procedure. The same may be said of Kraske's method, which should really be regarded as a modification of Hüter's. Kraske[101] recommends that numerous punctures and superficial incisions one centimeter long should be made in the inflamed skin. After squeezing the parts thoroughly, a solution of 2.5% carbolic acid is to be applied.

Gluck's[102] procedure is still more radical. He makes numerous incisions into the erysipelatous area which extend through the corium into the subcutaneous areolar tissue. As much of the edematous fluid as possible is removed by pressing and kneading. The skin is then thoroughly cleansed. Similar incisions are now made into the adjacent healthy skin and a 60% ichthyol ointment or solution is thoroughly rubbed into all the wounds. A thick dressing of gauze is then applied (Felsenthal[102]).

Riedel[103] anesthetizes the patient and makes bleeding incisions in such a way that one-half of the incision is in the healthy and one-half is in the diseased tissue. The incisions are from 6 to 8 centimeters ($2\frac{1}{2}$ to $3\frac{1}{4}$ inches) in length, at a distance of 0.5 centimeter ($\frac{1}{5}$ inch) from each other, and only of sufficient depth to draw blood. The parts are then covered with applications of bichlorid 1 : 1000, which are changed two or three times daily. Since this procedure leaves elevated scars, the author himself warns against its employment upon the face. We would advise against its use in all cases, since more conservative methods of treatment are undoubtedly to be preferred.

The great majority of physicians discard these more or less painful and unsparing procedures and prefer those methods which without doubt suffice in most cases. First among such treatments is the application of simple solutions or salves to the inflamed cutaneous surface. After repeated failures with those methods so enthusiastically advocated, no one could be blamed for discarding such radical procedures and employing this simple routine treatment. In the last few years I myself have returned to this resigned conclusion. To my mind, it seems best to cover the inflamed areas and their surroundings several times daily with pure vaselin or boric vaselin; if the patient prefers it, cool applications of boric acid solution, or weak solutions of salicylic acid or of lead-water, may be employed.

For a long time I have regularly wrapped up the parts in cloths soaked in a solution of bichlorid, without perceiving any advantage

over simple applications of boric acid solution or of salves. The latter treatment is almost always more agreeable to the patient.

On the face, the coating of vaselin may be well protected by a loosely fitting mask.

The ice-cap or applications of iced water are most suitable for the severe headache which is often present. Dry cups to the neck or behind the ears also exert an undoubtedly favorable influence.

If great restlessness, insomnia, and high fever are present, I prefer lukewarm (86° to 90.5° F.) baths with cold irrigations repeated two or three times daily to all other forms of treatment; under certain external conditions local or general cold packs must be substituted.

In laryngeal erysipelas, preparation must be made for an early tracheotomy.

I have practically discarded internal remedies. Mild purgatives or simple rectal injections are employed if there is constipation and the general nervous symptoms are very marked. The stronger purgatives, especially those of a drastic nature, are contraindicated, since a diarrhea of several days' duration may follow and further weaken the patient. If the headache is very violent, acetanilid (antifebrin) (gr. viiss) or phenacetin (gr. xv) is occasionally advisable, though these remedies may generally be dispensed with.

In people over forty, digitalis may sometimes be employed early. I give it in doses of 0.25 to 0.3 (gr. iv to ivss) daily for three or four days in succession, even if there are only temporary irregularities of the pulse-rate. If there is an alarming weakness of the pulse, camphor or ether may be given subcutaneously, or larger doses of digitalis may be necessary.

If stronger and more rapid effect is indicated, I would highly recommend Merck's digitoxin from an extensive personal experience. It is best given in doses of 0.25 milligram (gr. $\frac{1}{260}$) three or four times daily, and never more than for two days in succession. The remedy is then to be discontinued for a day. It should never be employed more than six, or at most eight days. The effect is often surprising. Kiliani's preparation, formerly known as digitophyllin, which "is closely related to digitoxin, but not identical with it" (Kiliani, *Archiv der Pharmacie,* 1897), acts in exactly the same manner.

If the deep stupor continues or symptoms of a beginning meningitis appear in spite of the baths and irrigations, local blood-letting or venesection may be considered; an attempt may also be made to relieve the intracranial pressure by means of lumbar puncture, although the procedure is only of temporary value. We have sometimes seen good

results from this operation, and have never seen it do the harm that is to be feared from every copious venesection.

It goes without saying, that every erysipelatous patient must be kept in bed. This is not only for his own sake, but also out of consideration for his fellow-creatures. We have already mentioned (page 436) that transmissions of the worst kind may occur if this is not observed; in the section on prophylaxis the unfortunate transmission of the disease by physicians has been considered.

The value of nourishment should not be forgotten. We are naturally governed by the fever. As much milk as possible may be given, also wine, and bouillon from which the fat has largely been removed. For the thirst, pieces of ice, cold tea, or large quantities of water flavored with fruit juices may be allowed. Carbonated waters are contraindicated, since they often puff up the stomach and intestine in a most uncomfortable manner.

[Apart from the management of the surroundings, dieting, and nursing of an erysipelatous patient, the following remedies have enjoyed a well-merited reputation while not attaining to the rank of a specific against the disease:

Tincture of perchlorid of iron, recommended by Hamilton Bell in 1851, has since then been given, especially in facial erysipelas, in full doses (20 to 30 minims) often repeated; that is, every second, third, or fourth hour. It may with advantage be prescribed with equal quantities of glycerin, and in peppermint or chloroform water. Mr. de Morgan, of the Middlesex Hospital, says that this treatment is most efficacious in shortening the duration of the attack and securing a rapid and satisfactory convalescence. He has given as much as an ounce to an ounce and a half of the official tincture in twenty-four hours, in the more severe forms of the disease. The ethereal tincture of the German Pharmacopœia, which contains 1% of ferric chlorid in a mixture of one part of ether and three parts of alcohol, is a favorite preparation in Germany under the name of "Bestuscheff's tincture."

In that country, however, quinin now enjoys a higher reputation, in consequence of the researches of Binz * and the recommendation of Liebermeister. When given in doses up to $4\frac{1}{2}$ grains every two hours, quinin reduces the fever and shortens the attack. A long experience leads me to recommend that quinin in such doses should be administered, not in acid solution, but mixed with milk or plain water. There is really nothing new in the quinin treatment of erysipelas, for long ago

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* *The Elements of Therapeutics.* Translated by Edward I. Sparks, M.A., M.B., Oxon. London: J. & A. Churchill, 1877. Page 206 *et seq.*

a mixture of ammonia and bark in effervescence was regarded as a sovereign remedy. Ninety grains of carbonate of ammonium in 6 ounces of decoction of bark, to be taken in ounce doses, effervescing, with half an ounce of fresh lemon juice every four or six hours, was a standard prescription.

M. Hallopeau * has employed and recommends the following method in the treatment of erysipelas with salicylate of sodium: (1) Application to the part of compresses wet with a solution of salicylate of sodium (1:20) covered with oiled silk and frequently renewed. (2) Internal administration daily of 4 grams (℥j) of the salicylate, in three doses, in weak grog. M. Bochefontaine's experiments have shown that if compresses wet in a solution of salicylate of sodium (1:20) be applied to a joint and covered with oiled silk, the drug will soon appear in the urine. Hallopeau begins the internal treatment with a calomel purge, and then gives sulphate of quinin and salicylate of sodium alternately, at a day's interval the one from the other.

The results of this treatment, observed in 12 cases, were as follows: (1) The temperature was undoubtedly lowered in those cases which presented marked febrile disturbance. (2) In most cases the duration of the disease was much abridged, judging from the statement of Vélpeau that twelve days is the usual course. In several cases the disease seemed quite promptly controlled. (3) Up to the time at which he wrote the author had not observed the accidents which have occurred within his knowledge in typhoid fever patients taking the same doses of the remedy. In one case there was a slight temporary delirium, which may not, however, have been due to the medicine. The author recommends suspension of salicylic acid treatment in this and other diseases as soon as cerebral disturbance or dyspnea makes its appearance.

The editor has himself followed this line of treatment in numerous cases of erysipelas, and with the happiest results, nor has he ever seen any untoward effects from the use of this almost specific remedy.]

2. THE TREATMENT WITH THE ANTISTREPTOCOCCUS SERUM (MARMOREK).

The brilliant success of the diphtheria antitoxin, so unanimously confirmed from all parts of the world, awakens the thought that the pathogenic influence of the streptococcus could be prevented or lessened

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* *L'Union Médical,* May 1, 1881, and *New York Medical Journal and Obstetrical Review,* September, 1881.

by a corresponding serum.   Marmorek[104] deserves the credit of having produced such a serum by his untiring labor at the Pasteur Institute. By regularly increasing inoculations of highly virulent streptococcus cultures in animals, he gradually succeeded in producing serums of increasing strength.

Chantemesse[105] was the first to report his results with this serum in erysipelas, and his conclusion was that this treatment "was productive of more favorable statistics than every other therapeutic measure." Within twenty-four hours, and seldom later than two or three days, he saw a distinct decrease in the redness, swelling, and pain. The desquamation was accelerated and occurred in large shreds. Sometimes the erysipelas continued to spread and halted only after repeated injections. The general condition quickly improved. It is said that, with sufficient dosage, the patient feels entirely well within some hours. The delirium disappears, the temperature rapidly falls, and the attack rarely lasts more than two or three days; the pulse becomes quieter and stronger. Albuminuria, if present, soon disappears—in a word, the severity of the disease is broken with a single stroke. The necessary dose is considered to be 20 to 40 c.c.

In 501 patients whom Chantemesse treated with Marmorek's serum the mortality fell to 2.59%. The cases treated with a serum of

$$1 : 7,000 \text{ gave a mortality of } 1.68\%$$
$$1 : 2,000 \quad \text{`` `` `` `` } 6.54\%$$
$$1 : 30,000 \quad \text{`` `` `` `` } 1.03\%$$

The last-named result is undoubtedly a very favorable one. But Bolognesi and Roger[106] have emphasized the fact that equally good results have been obtained "by the most simple treatments." The former saw in his cases an average mortality of 3.5%, which sank to 0.9% at certain times; the latter had a mortality of 3.43% in 609 patients.

From my own experience in the treatment of erysipelas with Marmorek's serum obtained directly from the Pasteur Institute, however, I must advise against its further employment at this time. My reasons for taking up this totally different standpoint are founded upon the following notes of two of my cases. In my opinion, they both demonstrate the absolute inefficacy of the serum, and the second case also shows that the most disagreeable after-effects may follow the employment of this remedy.

1. Anna L., servant girl, aged twenty-two, was admitted May 6, 1897, in a delirious stupor. She stated subsequently that on March 4th she was suddenly attacked by a chill, and shortly afterward noticed that her left cheek was swollen, red, and painful.

Upon admission there was an extensive erysipelas of the head and face. The exanthem covered the chin and extended to the middle of the neck. The skin over the forehead and root of the nose was wrinkled, since the disease had here run its course. There were small areas of necrosis over the zygomata and large vesicles filled with a clear brownish pus on the ears and chin.

The further course of the disease is shown by the temperature chart (Fig. 42).

In spite of four days' energetic and repeated treatment with the serum, the erysipelas extended to the neck, shoulders, arms, and down the back as far as the sacrum; the temperature and the pulse did not improve in any way and the deep stupor was of unusually long duration. The only perceptible change was that the albuminuria which had been present during the first four days disappeared during the injections.

2. Augusta M., servant girl, aged twenty-four, was admitted September 1, 1897, with an erysipelatous relapse. On August 23d she had developed a facial erysipelas which began in the left inner can-
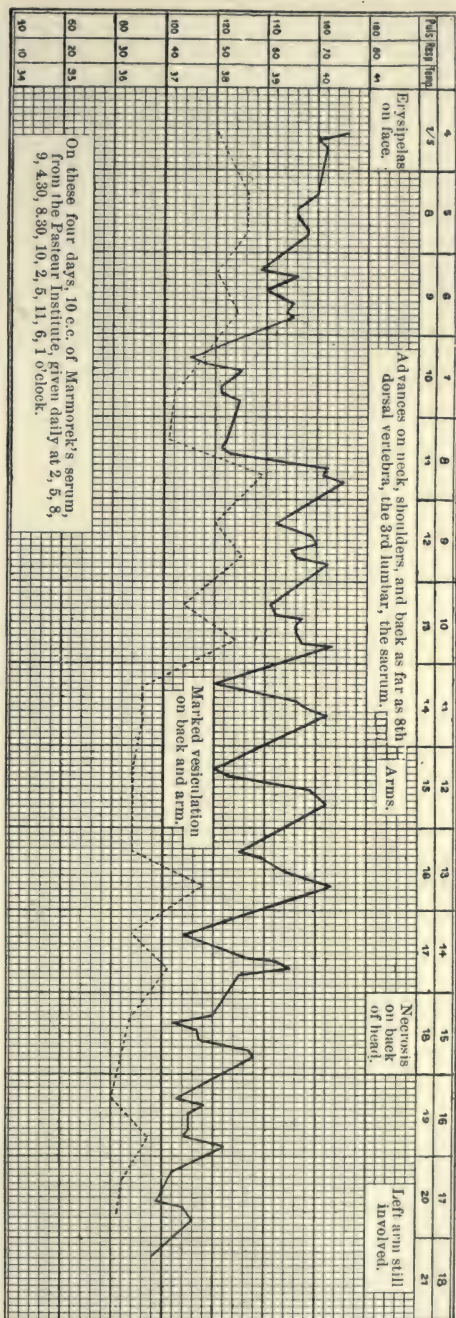
Fig. 42.

thus and then extended over both cheeks, and all around the neck. On August 29th she said "the disease was gone," and she felt so well that she left her bed. She had a chill, felt bad generally, and developed a new area of redness upon her back on the morning of August 31st. Upon admission the patient still showed desquamation on the cheeks and neck, and a fresh erysipelas upon the back. On September 1st this advanced to both shoulders. On both September 2d and September 3d, 30 c.c. of serum were injected, and on September 4th, 20 c.c. were employed. The injections were made in quantities of 10 c.c. at a time with several hours intervening between them. We also attempted to prevent the advance of the erysipelas by double strips of adhesive plaster about the arms. The erysipelas nevertheless involved the right elbow on September 5th and the right wrist on September 7th. It did not reach the left elbow until September 7th, and then stopped at this point.
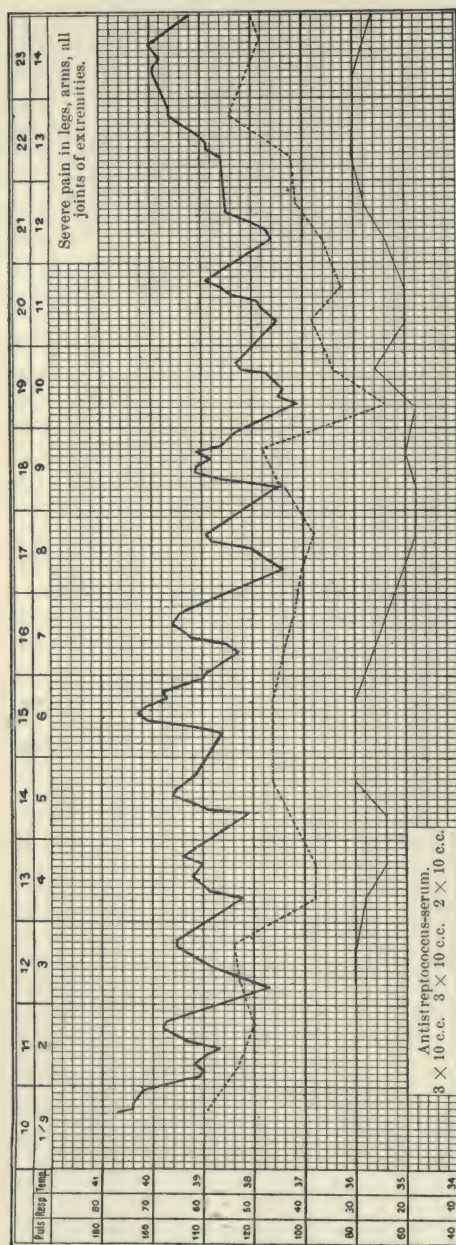
Her general condition commenced to improve September 10th, but two days later extremely disagreeable, and for a time most disquieting, aftereffects of the serum developed. These were manifested by high fever interrupted by chills, by a general exanthem, and by articular and muscular pains which daily increased in severity and distribution.

Fig. 43.

Antistreptococcus-serum.

3×10 c.c. 3×10 c.c. 2×10 c.c.

Severe pain in legs, arms, all joints of extremities.

The girl had the appearance of one afflicted with an unusually severe disease—no joint was spared! The intervertebral and the temporo-maxillary articulations were also severely involved. All the articulations were distinctly swollen and the joint outlines were completely obliterated.
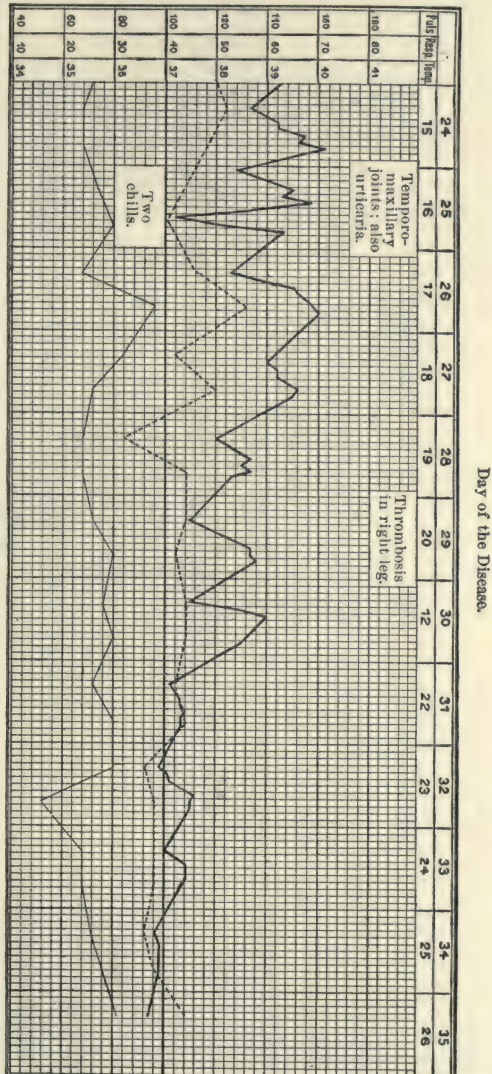
Fig. 44.

Every movement was anxiously avoided and the slightest touch caused an extraordinary amount of pain. The accessible nerve-trunks were markedly sensitive to pressure; the muscles showed a still more marked degree of tenderness.

The exanthem was introduced on the third day of this period by itch-ing and diffuse redness of the fingers and hands. On the next day there appeared numerous dots, wheals, and larger areas similar to the eruption of measles. On the arms these were limited in a very striking way to the area previously involved by the erysipelas. They were, however, seen on both surfaces of the trunk and upon the extensor surfaces of the lower extremities.

There were severe constitutional symptoms and frequent attacks of diarrhea until September 24th (twelve days!). The girl was not suffi-ciently recovered to be safely discharged until the end of October. The temperature curves are shown in figures 43 and 44.

After such an experience our unfavorable opinion of the thera-peutic value of the serum is still more justified by the fact that there was not the least evidence that it had exerted any favorable influence upon the erysipelas.

The previously mentioned case of R. Koch and Petruschky,[38] in which a typical erysipelas could be artificially produced 11 times in three and one-half months, also offered an opportunity to test the prophylactic value of inoculation with Marmorek's serum. Ten cubic centimeters of the antistreptococcic serum were injected twenty-four hours before the proposed inoculation with erysipelas. "The inocu-lations were nevertheless successful, and there was also no perceptible retardation of the course of the infection."

When examined from this point of view, we also fail to find evidence in support of the value of this remedy.

APPENDIX.

THE CURATIVE EFFECTS OF SPONTANEOUS ERYSIPELAS OR OF ERYSIPELAS ARTIFICIALLY PRODUCED (ERYSIPÈLE SALUTAIRE).

THERE have been occasional descriptions of the favorable influence of spontaneous erysipelas upon other diseases as far back as the seventeenth century. In addition to many nervous disturbances, neuralgias particularly, various cutaneous diseases, scrofulous glandular swellings, chronic articular troubles, and, what is of particular interest to us, malignant new growths, have been seen to disappear under the influence of erysipelas. The correctness of such observations is not to be doubted, since they have been confirmed in different diseases by the most reliable authors, and the permanent disappearance of visible or palpable diseases cannot be otherwise interpreted.

Cazenave,[107] Bazin,[107] Grivet,[108] and Hebra[109] have described the permanent cure of lupus nodules. Unfortunately, we cannot count upon this in every case, since Fehleisen states of a man aged twenty who had had lupus for twelve years that he had already had "many attacks of erysipelas."

Sabatier[110] declared that no remedy caused the phenomena of syphilis to disappear so rapidly as an intercurrent erysipelas. Ricord[15] saw even a phagedenic chancre rapidly cicatrized by erysipelas, and attempted to cure this condition by the artificial transmission of the disease. Maurice[111] and Lewin[15] were also convinced by an epidemic of erysipelas at the Charité that not only local and general syphilitic infection, but also indolent and suppurating buboes, were very favorably influenced by the disease.

It is also not to be doubted that erysipelas has caused the permanent disappearance of many tumors. In addition to other cutaneous tumors, epitheliomata, mammary carcinomata, and extensive tumors of the lymphatic glands, in all of which the diagnoses were correct, have been seen to completely disappear, and observations such as these must silence all doubts. It may readily be seen that attempts have been made to render such experiences of therapeutic value.

W. Busch[112] deserves the merit of having opened up a new path in this direction. In 1866 he had under his care a woman of forty-three years, who had numerous firm sarcomata—some of them as large as a

pigeon's egg—on the forehead, on the nose, and about the eyes. After an attempted extirpation of a portion of the tumors he saw an erysipelas develop under the influence of which all the tumors disappeared.

After Busch[13] had become convinced of this curative influence from a second similar case, he purposely attempted to transmit an erysipelas to a nineteen-year-old patient who had a large inoperable sarcoma of the cervical lymphatic glands. "There was in the clinic at that time a corner in a fine airy ward in which patients with open wounds could not be placed, because they were always attacked by some wound infection." The patient was placed in this bed after a dry scab had been produced behind the sternomastoid muscle. A week later a typical erysipelas appeared with temperatures as high as 40° C. (104° F.) and a pulse-rate of 120. The disease extended from the scab, over the left side of the face to the scalp, and then down the right side of the face to the neck in such a manner that the desquamation had already begun in the area first attacked when the disease still existed on the right side of the neck.

"With the first appearance of the erysipelas, and in spite of the cutaneous swelling, it could be distinctly noted that the tumor, which was previously very firm and elastic, now became very much softer and more doughy."

At the end of the second week, those tumor masses which lay between the sternomastoid muscle and the spinal column had completely disappeared; the chief tumor mass was also much smaller. This favorable condition, however, was not of long duration. "The last traces of the erysipelas disappeared and the strength of the patient quickly returned, but unfortunately with the returning strength there was a corresponding increase in the circumference of the tumor. Within a month's time it had attained its original size. A second transmission of the disease was without result, and the patient was not cured when she left the clinic."

Since that now celebrated attempt, which we have consequently given in some detail, there have been many repetitions of such a transmission. They are now much more easily carried out, since we, like Fehleisen, can introduce pure cultures of streptococci into the skin and produce erysipelas in the immediate vicinity of the tumor. Lately, the pure culture has been injected into the tumor itself, or the metabolic products of the bacteria have been utilized in the same manner.

From a collection of cases published by W. B. Coley[113] in May, 1893, I conclude that in 38 cases of malignant (recurrent and inoper-

able) new growths, to which an accidental or an artificial erysipelas was added, the following results were obtained:

Out of 17 carcinomata, 3 were cured, 10 were temporarily improved, and 1 died of erysipelas.

In 17 sarcomata, 7 were cured, 10 showed various grades of improvement, and 1 died of erysipelas.

Of the 7 carcinomata and 9 sarcomata purposely inoculated with erysipelas, 1 carcinoma and 2 sarcomata were cured.

In Petruschky's case[38] of inoperable mammary cancer, in which it was possible to produce a violent vaccine erysipelas 11 times within a comparatively short period, "no visible advance of the disease could be observed externally during this time, although none of the cancerous nodules disappeared and there was a decided failing of the general strength."

The outlook for the cure of such diseases by erysipelas is consequently very dubious. Nevertheless no objections can be made against such efforts, since otherwise such cases are surely lost.

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ERYSIPELOID.

(ZOÖNOTIC FINGER ERYSIPELOID, ROSENBACH.)

UNDER the name of zoönotic finger erysipeloid, Fr. J. Rosenbach has described a peculiar wound infection, which, in the words of this investigator, "has very little significance because it is a very innocent disease, but nevertheless deserves consideration because, in the beginning, it may be confounded with more severe infections."

Clinical Description.—Erysipeloid affects particularly those individuals who have to do with meat, game, poultry, oysters, cheese, herrings, and the like, or those who are employed in flaying and tanning. We consequently find that cooks, inn-keepers, butchers, and dealers in game, fish, and oysters are most frequently attacked by this disease. Since the disease is never accompanied by fever, it is only exceptionally seen in hospitals. It is, however, rather frequently observed in dispensary practice. In 1885 Cordua reported 127 characteristic cases which he had observed during five years' service at the Policlinic of the General Hospital in Hamburg. The average number of patients treated yearly was between 4000 and 5000, and, according to this author, erysipeloid was observed about 20 times a year.

The disease is chiefly seen in the fingers, since these members are particularly likely to come in contact with the previously mentioned animal substances. Other cutaneous areas are undoubtedly attacked; the cheeks, especially, are sometimes involved.

On the fingers, the disease commonly commences at the terminal phalanges. A dark red almost livid swelling, with quite a sharp border, like erysipelas, is seen to extend from the extremity of the digit. The patient experiences a most annoying sensation of itching and tingling in the reddened area. The general condition is not disturbed, and the body-temperature in particular is not affected.

The elevated and sharply defined redness advances very slowly, and does not reach the metacarpus until about eight days after its appearance upon the tip of the finger.

After another eight days the back of the hand may gradually become involved, or the exanthem may creep forward to the end of the neighboring finger.

As a rule, the disease ceases spontaneously within one, two, or three weeks, the areas first attacked becoming paler as the redness advances.

If erysipeloid occurs upon the face, it usually extends from the nose to one cheek; very rarely, there may be a bilateral extension to both cheeks, like the wings of a butterfly. There is present a marked bluish-redness and more or less swelling with itching or painful tension.

Since the general condition is not disturbed, the patients often go about as usual, but their ability to work is not rarely impaired by the marked swelling and throbbing of the fingers and back of the hand.

Etiology.—Although the disease is tolerably common, there is as yet no series of bacteriologic examinations which is not open to objection. Fr. J. Rosenbach in his first communication (1884) spoke of "small but irregularly shaped cocci," while in 1887 he described "peculiar thread-like microbes, which are probably a species of cladothrix." His microbe grew best upon gelatin at a low temperature. Auto-inoculation on the left arm was followed within two days by redness and itching. On the fifth day there was an area of redness, as large as a dollar, surrounding the field of inoculation, which was somewhat elevated, sharply circumscribed, and the seat of marked itching. While this central area paled, up to the point of inoculation, the affection spread about an inch toward the periphery. There were irregular, roundish districts showing the bright color of capillary injection with a brownish tinge added, while a brownish livid color was observed inside and outside of the zone. "The color of the center was yellow, while that toward the ring was bluish-yellow and resembled a bruise." After a temporary paleness the burning sensation was renewed upon the ninth day, and a larger ring appeared, so that the area involved was 10 centimeters long in the axis of the limb and 17 centimeters transversely. Nine days later the area measured 18 by 24 centimeters. The exanthem then disappeared. The general condition and the body-temperature remained undisturbed.

Microscopic examination of gelatin cultures revealed thick swarms and clumps of irregular roundish and elongated bodies larger than staphylococci. Curiously twisted threads appeared later, which had developed from those structures regarded as cocci.

Cordua excised a piece of skin from a living patient under antiseptic precautions and put it into agar. After twenty-four hours at a temperature of 36° C. (96.8° F.) there was a broad white growth from the edge of the piece of skin. This was a pure culture of a coccus.

The circumference of the coccus was between three and four times greater than that of the Staphylococcus aureus. Auto-inoculation was followed by the appearance of a dark red spot as large as a quarter or a shilling; itching was the only disagreeable symptom, and the red-

ness disappeared in a few days. Small pieces of skin were also excised and placed in agar; they furnished colonies of the same coccus.

Felsenthal cultivated what was probably the same coccus in three cases of erysipeloid by placing excised pieces of skin in fluid gelatin and keeping them at a temperature of 18° to 20° C. (64.4° to 68° F.). After a few days a peculiar flocculent cloudiness of a silver-gray color developed in the bottom of the culture-medium. The cocci were distinctly larger than the staphylococcus.

The demonstration of the germ in sections is still wanting. I know of but one examination, that of Delbanco, which was most carefully carried out and resulted in the finding of no bacteria whatever. Delbanco found the interepithelial spaces widened and sparingly filled with leucocytes; the prickle cells were succulent and their protoplasm did not stain very well. There was an edema of the cutis which decreased toward the papillæ. The papillæ were broadened and rounded off.

The most striking feature of the sections to Delbanco was the richness in mast-cells, which were to be seen in the follicles, at the edge of and within the columns of perithelial cells, and also in the tops of the papillæ. In certain localities the lymph spaces were dotted with the free granules of mast-cells. Many mast-cells showed their specific stain in only one portion of the slightly swollen protoplasm. Here and there ruptured mast-cells were seen from which the granules had escaped.

The most varied bacteriologic staining methods were employed for the sections, but only a negative result was obtained. Further careful investigation of the exciting cause of the disease is consequently necessary.

Diagnosis.—As a rule, the recognition of the disease is easy and certain. The pronounced tendency to localization upon the hands and fingers, the preference for those persons who come in contact with the previously mentioned animal substances, the bluish-redness of the exanthem, the complete absence of fever and other constitutional symptoms, usually allow the careful observer to make the diagnosis at a glance.

Nevertheless, confusion with erysipelas undoubtedly occurs. As previously stated, erysipeloid may also appear upon the face, and in this case a wrong diagnosis will frequently be made. The error is the more pardonable if the alæ of the nose are reddened and thickened and if the sharply outlined redness and swelling creep over one or both cheeks. Fever is absent, however, as is every other disturbance of the

general condition. The exanthem itself has neither the bright redness nor the glistening appearance of that of erysipelas, and tension and itching are the only sensations present. In my experience these cases are chiefly responsible for the supposition of an *afebrile* facial erysipelas.

The possibility of the occurrence of erysipeloid in other situations than the fingers, the seat of predilection, must undoubtedly be admitted, if the infectious origin of the disease is recognized. Small cracks and fissures are frequently present in the neighborhood of the nose, or about the face generally, into which the disease germs may be rubbed by dirty hands. The appearance of the exanthem on the face is consequently not surprising, when we remember how often such individuals pick their noses or scratch their faces with their infected hands.

Erysipeloid is much more rarely confounded with erythema multiforme. The differential points to be remembered are that erysipeloid always begins in but one situation and slowly advances, while erythema multiforme as a rule appears in several areas of skin, is usually symmetric, and is not rarely accompanied by considerable fever.

The **prognosis** of the disease is very good. The affection often ceases spontaneously after five or six days; in less favorable cases it may not disappear until after two or three weeks. A change of occupation is not necessary, since recurrences of the disease have not been observed.

The **treatment** should consist in the application of simple ointments or of boric acid solution and a protective dressing.

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WHOOPING-COUGH.

BY

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WHOOPING-COUGH.

HISTORY.

In the spring of 1578 an epidemic spread over Paris which, according to Guillaume de Baillou's report on the epidemics and medical events of that year, was likened by the medical men to the "coqueluche" of the older writers, and undoubtedly showed many points of resemblance to it. Raging headache, incessant irritation of the throat giving rise to continuous coughing not amenable to treatment, high fever, intense inflammation of the eyes, and pains in the chest, chiefly on the left side, were the most striking symptoms.

In the middle of summer of the same year after an interval of a couple of weeks another cough epidemic broke out, but this time principally among children between four and ten years of age. It was called popularly "quinte," and by the physicians "quinta" or "quintana." These names arose from the onomatopoietic resemblance of the word "quinte" to the sound of the cough, as Ballonius suggests, or from the recurrence of the paroxysm every five hours—*est enim numerus certus pro incerto;* or in order to differentiate the musical pitch of the cough *in faucibus* from the tone of the cough *in profundo pulmonis editi.* The erudite Jacobus Dovinetus in his "Apology" sought a deeper signification for the "tussis nova Lutetiæ, quinta dicta, pueros comprimis infestans; quod quemadmodum quinta essentia erutu difficilis est, sic et hæc tussis sanatu difficillima est." At least Joannes Schenckius so quotes him in the second book of his "Observationes Medicinales."

In the recurring paroxysms of quintana, nothing was coughed up even with the most violent efforts, but blood flowed from the mouth and nose, and the stomach emptied itself completely. During an attack the patient seemed to swell, and looked as if he were on the verge of strangulation. At the end of the cough a large amount of mucus or purulent material was expectorated. Innumerable children were swept away by this pest.

Ballonius was acquainted with no writer that described before himself the cough and the "hommes quinteux." Yet he says that he was informed the name "quintana tussis" had been met with in print in some author or other.

We have been unsuccessful in discovering this author.

De Baillou appears not to have known Lævinus Lemnius, otherwise he would surely have differentiated his quinta from the cough which this Belgian physician mentioned in 1561 in the third book "De miraculis occultis naturæ" as a well-known incurable cough called in Belgium "Kindthoest": "quod singultu quodam prodeat, nullis admissis induciis

aut respirandi spatio. Cum enim continenter ac laboriose nullaque interposita mora tussiunt: irritus tamen est conatus, nec quicquam proficiunt, adeo ut intercepto occlusoque anhelitu suffocatio immineat atque obturatis spirandi fistulis anima ac spiritus, qui ultro citroque commeat ac reciprocatur, postico prodeat erumpatque." It is evident that this "tussis pueros strangulans" is not the quinta of Ballonius, but rather the croup of Home and the chin-cough of Sennert.

But the historic writers on whooping-cough differentiate so little individual "coughs" that they reckon as whooping-cough every disease associated with violent coughing that has been described. Even Ballonius, who differentiated so carefully his coqueluche and quinte, is not entirely free from this fault, since he refers to a sentence on erysipelas of the lung in Hippocrates' first book περὶ νούσων, which he believes to be a description of quinta.

Many physicians following him have likewise endeavored to untomb tussis quintana in the oldest writers even as far back as Hippocrates, but without result. They have simply shown their tireless zeal in seeking rather than their intelligence in interpretation. Whoever follows them to the original sources must be surprised at the childish simplicity, nay, even foolishness, that they display in making every cough mentioned by ancient writers the quinta of Ballonius.

We therefore refrain from worrying the reader with individual references to Greek, Roman, and Arabian writers, and only desire that future monographs on whooping-cough will omit as unproved padding references carried through all books, and with especially indefatigable diligence and conceit by August Hirsch and Biermer to the actual page in "Hippocr. epidemior.," lib. VI, sect. 7, lib. VII, etc.; "Hippocr. aphorism.," sect. 6; Avicenna, lib. canon. III; "Mesuë canones univers.," "caput de ægritud. pectoris et pulmonum," etc., in order that subsequent authors, like many of the present day, may admire their erudition. Because the places referred to contain only the word "cough" or "violent cough," and so everything further that might constitute "cough," whooping-cough is to be surmised or added.

The passage in the sixth book on "Epidemics" seems to us one of the best descriptions of an epidemic of diphtheria. The son of Amphiphrades in the seventh book died of a clear attack of empyema, and Hippocrates saw in him no symptom of whooping-cough. And how the aphorism ὁκόσοι ὕβοι ἐξ ἄσθματος ἢ βηχὸς γίνονται πρὸ τῆς ἥβης ἀπόλλυνται can refer to whooping-cough is inconceivable. For is it true that many children, or children in general, become hunchbacked on account of whooping-cough and die before puberty? Or have learned scholars like Danz, whose judgment appears at best but trivial in his compiled book; like Marcus, who repeats only Danz and Whatt and Badham; like Haase, who scarcely stands out independently; like Desruelles, who fearlessly adds gratuitously to the words of Hippocrates in order to make them intelligible to the reader—have these learned scholars discovered a hunchbackness for whooping-cough to correspond with this aphorism? Did they not feel how little honor they added to the greatest, truest nosographer when they tried to point out de Baillou's quinta in his works?

It is remarkable that no writers encountered the fourth chapter in the second book, "De symptomatum causis," of Galen, otherwise the βίαιοι βηχές would serve as a proof that Galen also recognized whooping-

cough. This chapter speaks of every imaginable kind of a cough, except an epidemic one. That the much-spoken-of βήξ θηριώδης (*tussis ferina*) of Hippocrates signifies many others, yet no epidemic cough of childhood with frequently recurring paroxysms, can be unequivocally affirmed from the second book of Galen's "Commentaries" on the sixth book of "The Epidemics" of Hippocrates.

Therefore it may be taken as settled that Oribasuis and Ætuis, Celsus and Plinius, Avicenna and Mesuë, as likewise the Byzantines, Romans, and Arabs, knew absolutely nothing about whooping-cough.

It was, moreover, unknown to the physicians and writers of the middle ages. Everything at least that Mézeray, Danz, Ozanam, Schnurrer, Desruelles have taken from the chronicles of the Capucins at Paris, the Buoninsegni at Florence, of Giovanni Villani at Florence, Estienne Pasquier at Paris, everything that appears in the writings of Valesco, Schenckius, Valleriola, Vidus Vidius, only proves that during the thirteenth, fourteenth, and fifteenth centuries in France, especially at Paris, Saint-Denis, and Montpellier, and in Italy, especially in Tuscany, Florence, and Siena, epidemics took place which either altogether forbid identification because no description was left except a brief statement as to their great fatality, or which must be regarded as epidemic laryngeal catarrh, or as croup, or grippe, or plague whenever the symptoms are at all adequately presented.

The symptoms of quinta which Ballonius points to in his autumn epidemic and differentiates so minutely—even if perhaps not altogether with the consciousness of the specific distinction—from the picture of coqueluche in the spring epidemic, are to be found in no previous writer, while the name "coqueluche" can be traced to Mézeray in 1414, and was used by Ballonius and his predecessors to indicate not whooping-cough, but always, or at least usually, influenza, and in one exceptional instance an epidemic summer catarrh.

Listen only to the much-quoted account of Pasquier: "Es registres du parlement on trouve que la 26e jour d'Avril 1403 il y eut une maladie de teste et de toux, qui courrut universellement si grande qu 'en ce jour-là le greffier ne peut rien enregistrer, et fut-on contraint d'abandonner le plaidoyé; tout ainsi que nous vismes en l'an 1557 en plein été s'effleurer par quatre jours entiers un reume qui fut presque commun à tous, par le moyen duquel le nez distillait sans cesse comme une fontaine avecques un grand mal de teste et une fièvre: laquelle maladie fut depuis par un nouveau terme appellée par nous coqueluche."

The epidemics of 1403 and 1557 can positively be separated into influenza and catarrhus epidemicus, and should not be grouped together as Pasquier insists. As to the origin of the word "coqueluche," we read in Valleriola (*in appendice ad enarr. medic.*): "Coculuche, quod qui morbo tenebantur, cucullione caput velarent. Abitrabantur enim a cerebro in pulmones fluxionem irrumpere, caputque cucullo tegentes putabant se sic melius habituros." Subsequently other authors asserted that the word came from "coquelicot" [that is, wild poppy], because opium was found efficacious in the cough of coqueluche; still others, referring the name to whooping-cough, found the origin in "chant der coq," since the cough resembled somewhat the crowing of a cock. In any case it was employed between 1414 and 1578 in quite a different signification to that of quinta; it then disappeared till 1724, when it was

again taken up, to serve from that time to our own day as a designation for the old quinta, our whooping-cough.

The above-mentioned Pasquier records a further epidemic of coque-luche in 1411, while Valesco refers the same, though very indefinitely, to the previous year. The latter describes it as raging in Paris *par le plaisir de Dieu* at the beginning of March, 1410, and as attacking more than 100,000 people within three weeks. According to Pasquier, the disease began with prostration, a sensitiveness of the skin that forbade the slightest touch,—"que on n'osoit toucher à soi de nulle part que ce fut,"—fever, distaste for food, and a cough so violent both day and night that many patients developed herniæ and some pregnant women aborted. At the crisis there appeared frequently a profuse hemorrhage from the mouth, nose, and anus. There was scarcely any mortality. The epidemic, which no one attempted to explain, was called "tac," and "horion." Common people believed it to be the punishment of God for the general singing of a very free and easy ballad. Consequently, patients were teased with: "Ha! ha! you will sing the ballad, will you?" ("En as-tu? Oh! par ma foy tu as chanté la chanson!")

And this, according to some of our illustrious historians, was whooping-cough.

The distinguished Schnurrer opines that "tac" must not be considered the same thing as the catarrh which raged over France, but especially Paris, in February and March of 1414, because this time it was called coqueluche, was characterized especially by hoarseness, and, as Mézeray mentions, it broke up all judicial business and the collegiate courses.

"Un strange rhûme," says the last-named historiographer of France, "qu' on nomma la Coqueluche tourmenta toutes sortes de personnes durant les mois de Février et de Mars et leur rendit la voix si enrouée, que le Barreau, les Chaires et les Colléges en furent muets. Il causa la mort presque à tous les viellards qui en furent atteints" (1414).

This is again not whooping-cough. And the "ladendo" of Pasquier and "la dando" of Ozanam in 1427 are no more so.

What becomes of the famous epidemic of whooping-cough that spread over the whole known world in 1510, when Holler designates it as epidemic headache, in which "parotides supervenerunt cum magna strage hominum," and when Thuanus describes it, like Holler, under the name "vervecine"? Added to this, Mézeray completes the picture, so that it seems scarcely possible for a thought of the quinta of Ballonius to occur: he says that with the headache there were pains in the region of the stomach, the kidneys, in the thighs, associated with high fever and delirium, that on the fifth day a catarrh with expectoration set in and lasted till the tenth day, and during this time the prostration, aversion to food, especially meats, and sleeplessness continued.

According to Fernelius, "illa omnibus decantata gravedo anhelosa, anno Christi 1510 in omnes fere mundi regiones debacchata, cum febre, cum summa capitis gravitate, cum cordis pulmonumque angustia atque tussi, quanquam multo plures attigit quam jugulavit, se suo tamen impetu proprioque ac inaudito veneni genere pestilentem prodidit." But as to the observation of some investigators, that "according to Fernelius the mortality was confined almost entirely to children," no such idea is to be found in his whole treatise. Thus it is to be re-

marked again how the trail of whooping-cough is associated with mental delusion.

In July, 1557, an epidemic broke out in Europe, especially in Germany, France, Italy, Spain, and Holland, which Riverius and Pasquier, Mercatus, Dodonnæus, Ingrassias, Forestus, Schenckius, Stenglinus, Sporischius, Bockelius, Salius, Marcellus Donatus, Valleriola, and Joannes Bauhinus described partly under the name "coqueluche," again as catarrh, pleuritis, tracheitis, but always with symptoms that by the broadest application could not be quinta,—that is, whooping-cough,—even when called by this name: "subitaneam quasi inferens suffocationem" (Forestus), or "catarrhus cum cephalalgia, gravedine anhelosa et tussi epidemica" (Schenckius).

With the maximal easterly deviation of the magnetic needle in 1580, an epidemic took place which after a hard winter began in the middle of summer in the east, spread to Italy, and shortly afterward appeared simultaneously in many places in Europe—in Rome, Tübingen, Delft, Paris, and London. It was known under different names by different writers, who also vary somewhat in their descriptions. In Germany it manifested serious suffocative symptoms, and from the name employed on account of the conspicuous symptom of laryngeal obstruction, officiously enterprising writers, like Desruelles, manufactured another famous epidemic of whooping-cough. Daniel Sennert's treatise "De catarrho et tussi epidemica maligna" is sufficient to prove this conclusion false: "Totam fere Europam imo fere omnes mundi regiones pervagata est et hinc inde varia nomina accepit: appellabatur enim catarrhus epidemius, tussis epidemia, cephalalgia contagiosa. Germani nominabant den Ziep, den Schaffshusten, die Schaffkrankheit, das Hühnerwehe, quod aegri instar gallinarum coryza vexarentur. . . . Quamvis tussis non diu durabat, tamen illa anhelitus difficultas ad diem XIV. extendebatur; nonnullis sudor superveniebat, qui die XXX. vel XL. convalescebant. . . . Et quamvis maxima hominum pars hoc malo corripiebatur: omnes tamen fere evadebant et vix millesimus quisque moriebatur." In Rome, however, two thousand persons died, yet not of the disease, but of venesection badly and too frequently carried out. At least this is the judgment of the physician Wierus, who described the disease as "tussis pestilentialis et epidemica."

Moreover, the epidemics of 1590 at Rome, 1593 in France and Italy, 1627 at Naples, were anything else but whooping-cough. If Nils Rosén von Rosenstein and August Hirsch are correct when they affirm that the history of whooping-cough cannot be traced beyond the middle of the sixteenth century, then it may be added that from 1578 to 1658, from Ballonius to Thomas Willis, no true whooping-cough epidemic was described, and therefore none must have occurred.

The second historic whooping-cough epidemic broke out in London in 1658 during the last days of April after a winter in which the snowfall was extraordinary; the disease lasted six weeks and disappeared. The designation bestowed on it by Willis should without further investigation leave no doubt as to its identity. He calls it "tussis puerorum convulsiva seu suffocativa et nostro idiomate Chincough vulgo dicta" in his treatise "De medicamentorum operationibus" (Sect. I, cap. 6). The disease must at that time have been endemic, and only now and then have shown its epidemic climax: "quibusdam annis ita plurimos corripit ut plane epidemica videatur" is said by him in the book "De

morbis convulsivis" (cap. 12). It could "vix aliter nisi ab immutato anni statu curari."

From the middle to the end of the seventeenth century the reports on actual epidemics of whooping-cough are rare, and contain much that is erroneous.

Sydenham mentions in his treatise on the morbilli or measles of the year 1670, "Infantum pertussis, quem nostrates vocant hooping-cough." And in 1679, he differentiates very accurately and cleverly from "tussis puerorum convulsiva"—a cough epidemic in which vomiting, long and fruitless paroxysms of coughing, and dizziness were the most prominent symptoms—"ad tussim puerorum convulsivam mihi propius accedere videbatur, nisi quod mitius aliquantum sæviret. In hoc saltem convulsivam superabat, quod et febre et solitis eius symptomatibus stipata ægrum invaderet, quæ in tussi puerorum nondum me vidisse memini."

In the year 1695, after a long winter that began in October and ended with the thawing of the Danube in March, there occurred a disagreeable summer, which brought with it a wide-spread cough epidemic that proved fatal to numerous children at Rome and Paris. Schnurrer calls it quinte, and compares it with de Baillou's epidemic. Yet, according to the descriptions, it may have been either whooping-cough or an epidemic bronchitis. The "febris catarrhalis epidemica," the "disease *à la mode*" of the year 1712 reported by Camerarius of Tübingen, has, judging from its description, nothing in common with whooping-cough, Danz to the contrary notwithstanding.

According to Schnurrer's chronicle, the year 1724, a splendid wine and fruit crop year, was healthful except for an outbreak of whooping-cough in England and the Asturias. This was characterized by the violence of the cough in contrast to previous years. No child over seven years of age was attacked. Huxham investigated it in England and left an excellent description; Ozanam reported in the same year an epidemic in Alsace.

Antonius Guilelmus Plaz gives an accurate and minute description of "tussis infantum epidemica" as occurring in western Europe in 1727 in his Inaugural Dissertation, published under the direction of Professor Michael Albert in Halle a year later. He was acquainted with the quinta of French physicians, for, though he quotes no writer, he says that in eastern Germany "tussis convulsiva" is much more frequent than in France, and he mentions a "tussis parallela" which Reinmann describes in the Historiis Vratislaviensibus (XXXV): "This disease attacks usually small children, particularly those intra primum annorum septenarium": "adultiores" very seldom, principally because this "ætas humidissima est."

"Tussis epidemica constituit," according to Plaz, "utplurimum magis morbum quam symptoma morbi: est itaque hæc tussis vehemens pectoris et pulmonum succussatio, cum profunda et anxia aëris retractione et subitanea efflatione necnon suffocatorio-spastica comminatione et eximio clangore et sonitu, suffocationis punctum referente, ut et exspectoratione multæ spissæ tenacis materiæ flavescentis, quasi purulentæ, interspersis nonnumquam cruentis stigmatibus conjuncta, a certa aëris intemperie excitata, per intervalla et instar paroxysmi sæpius irruens, proinde diuturnum decursum servans, anomalos motus febriles provocans, sæpius etiam purpuram, cutaneas inflammationes, lentem febrem, imo aliquando hecticam et mortem pedisequas habens."

This is our whooping-cough, and but little is wanting in the picture. Further particulars were added in a Halle Dissertation, published four years later, by a pupil of the great Friedrich Hoffmann, Samuel Pitsch: "De Tussi convulsiva," or cough associated with a general spasm.

More precise than Sydenham, Pitsch refers to the relation between morbilli (measles) and tussis convulsiva.

In the year 1732 appeared the celebrated description by Hoffmann himself in the "Systema medicinæ rationalis." He had already written on the disease a postscript to the dissertation of his pupil. The epidemic of 1732–1733, as far as can be learned from the writers of that time, raged over Europe as a pandemic, and wound up in Jamaica, Peru, and Mexico.

Though Boerhaave, so far as we can see, fails to mention whooping-cough, de Haen describes very accurately in his lectures on this great teacher's work an epidemic at The Hague in 1746–1747.

Omitting the records of small epidemics, we come next to the admirable reports on the large epidemics of 1749 in Tübingen by Sauvages, 1749–1764 in Sweden by Rosén von Rosenstein, 1755 in Switzerland by Zwinger, 1763 on the island of Oeland by Wahlbom, 1769 in Germany by Mellin, 1770 in Brunswick by Holdefreund, 1815 in Milan by Ozanam, etc. In the nineteenth century no year has passed without one or more communications on small epidemics.

But the outbreaks of our day in civilized countries act within always lessening circles, and for the most part assume such an indefinite origin that the disease seems to be quite endemic, and would rarely be spoken of as epidemic pertussis, were it not that here and there in newly discovered countries, or countries recently colonized by cultured Europeans, the tussis convulsiva transmitted by them has been revivified and has become again capable of epidemic ravages.

GEOGRAPHIC SPREAD.

We repeat that a disease with such distinctive, striking symptoms and so characteristic a course as whooping-cough could not be overlooked by the vigilant observing minds that since Hippocrates correctly diagnosticated the most masked diseases and clearly differentiated so many different ailments. The history of whooping-cough therefore begins with its first unequivocal description, and as long as no demonstrable and indubitable passage can be shown in the writings of earlier physicians, we must refer its commencement with certainty to de Baillou.

Yet the origin of the disease must remain shrouded for all time, since we have received not the slightest conjecture from Ballonius, his contemporaries, or successors as to how the focus arose from which the autumn epidemic of the year 1578 at Paris spread. There is nothing to indicate even that the epidemic began in Paris, because the fact that

it was described there alone, signifies only that there was no one else-where who observed it with the proper epidemiologic interest.

Whooping-cough at the time of Thomas Willis was doubtless a well-known pest in England, and the London physician failed to dis-cuss its origin both on this account and because of all the things that we have from his pen he showed least concern as to the history and geographic spread of epidemics and diseases in general.

If we collect the records from the latter half of the seventeenth and first half of the eighteenth centuries, and with their aid present graph-ically on a map the topography of whooping-cough, we find undoubted confirmation of those writers who asserted that the home of the virus is in the north coast-lands of Europe. Perhaps, too, as Schönlein in-sinuates, foci arise in the northern and southern fresh-water basins of Switzerland, like intermittent fever or cholera, and spread thence along the course of the rivers, most probably in connection with the traffic on them.

In the years 1658, 1669, and 1670 whooping-cough raged in Lon-don. In 1724 it was observed in Germany and in many places in Switzerland. In 1732 and 1733 it spread over the whole of Europe and was carried by English ships to the coast of the American continent, where the epidemic soon ceased. In 1745 to 1748 it ravaged Sweden and the bordering countries, and the Swedish observer Rosén von Rosenstein, and likewise Matthaei, are of the opinion that it was intro-duced there from Africa or India. But they give no reason for the opinion. At the middle of the eighteenth century we find pertussis as a well-recognized disease over the entire European continent, as well as in many extra-European countries, and we find it described in all treatises on pathology.

In our time the disease has continued to extend its area of prev-alence. It is now found endemic in the Scandinavian Peninsula, Denmark, Russia (from St. Petersburg to the Caucasus), Germany, the Netherlands, Belgium, France, the British Isles, the Iberian Penin-sula, and Italy. Yet it always appears to prefer northern to southern Europe.

In North and South America, as in northern Europe, whooping-cough has become an annually recurring disease. The Esquimos in the territories of the Hudson's Bay Company have been so far ex-empt, although the North American Indians are frequent sufferers. According to Danish reports, it is endemic in Greenland (Hirsch). It is found in the West Indies, and since 1846 in California. The ele-vated plateaus of Texas seem to be immune. As in Central America,

so in the Asiatic and African tropics, but little is seen of whooping-cough, and it is probable that all cases occurring there have been introduced. On the sea-coast of every continent it is endemic.

The disease was imported to New Zealand, according to Thomson, in 1847. Only within the last ten years has it been transplanted to the Australian continent and archipelago, where, according to Gibbs, it is dreaded as a frequent and very pernicious disease.

Whooping-cough in our day possesses no definite limited endemic area of prevalence, like yellow fever, for instance, or cholera. Still, this proves nothing for past times, since even the bacillus of cholera, at least according to von Pettenkofer's opinion, coming from Asia, has produced a culture-ground in Europe. Moreover, the facts that even now the Faroe Islands and Iceland are visited only after a fresh introduction of the infection, that Australia and Tasmania have known the disease only since the thirty years' epidemic, and the Sandwich Islands and New Zealand only from ten to twenty years later, point to the conclusion arrived at by Hirsch, that the home of whooping-cough is by no means so extensive as its geographic distribution.

It is to be regretted that it can no longer be determined whether the foci of the disease are grouped closer together in northern Europe than formerly, or whether this is only a probability. The number of physicians, and consequently of reporters of diseases, has increased to such an extent that the slightest suspicion of an epidemic scarcely ever escapes description; and, again, scientific circles have so busied themselves over the smallest nosologic facts and theories that if we judged of the geographic spread of a disease from the number of writers, Berlin, for example, would take the first place in general morbidity and likewise in whooping-cough.

In any case, a thorough investigation of all articles quoted by Hirsch or published later would be necessary to determine, in addition to the spread of the disease, the intensity of its spread, and to ascertain certain points, from which as foci the epidemics sprang.

There is no doubt that the severity of epidemics in Europe has decreased with the more general dissemination of the disease. To prove this it is only necessary to read the old and recent reports. And though actual figures may be wanting, the statements alone are sufficiently convincing. The last pandemic in Germany was in 1815–1816. Since then the annual mortality from whooping-cough among children corresponding to the density of the population, though it is greater than desirable, is small in proportion to the general death-rate among them. In 1851 in Frankfort 3.54% of the mortality in children was

due to whooping-cough. In Berlin from 1838 to 1847, it was only 1.9%, and the entire number of deaths attributed to this disease in these ten years was 800 (Biermer). Likewise in other countries the mortality is comparatively slight. England alone shows high figures. In 1877, among 500,341 deaths there were 10,318 caused by pertussis, therefore 2% (Lee). In London from 1838 to 1853, 838,751 people died in all, and among these 28,766 children of whooping-cough, therefore 3.4% (Gibb); and from 1821 to 1835 among 332,708, 11,269 of whooping-cough, therefore 3.3% (Hamilton, Roe). Yet these high figures prove nothing in support of Biermer's opinion that the mortality of pertussis has increased in England since the thirties. For the fact that between 1821 and 1835, 11,269 children died of whooping-cough and in the interval between 1838 and 1853, 28,766 died, means only that since 1830 London enlarged considerably, and, again, the statistics became more accurate. While the city in 1821 numbered 1,200,-000 inhabitants, twenty years later it had (according to Schneider and Keller's "Handbuch der Erdkunde") over 1,870,000 inhabitants.

In England and Wales from 1838 to 1842, and from 1847 to 1849, —that is, in eight years,—65,381 children succumbed to whooping-cough, while, for example, the less populous Sweden lost in the great epidemics of 1749 to 1764,—that is, in sixteen years,—43,393 (Rosén von Rosenstein), and from 1806 to 1830,—that is, in twenty-five years, —50,882 children (Gibb). At that time England had 18,000,000 inhabitants, while Sweden had in 1749 only 1,746,449, and in 1800 only 2,347,303 (Daniel's "Handbuch der Geographie").

The period necessary for whooping-cough, after it has become endemic, to take on epidemic features, or at least to increase in virulence, is, according to the scanty facts which can be gathered from the literature, about three or four years.

In relation to this, Huxham observed epidemics at Plymouth in 1732, 1739, 1743 and 1744, 1747; in the Netherlands there were epidemics in 1747, 1750, and 1751 (Marcus); in most places in Germany in 1768 to 1769, 1772, 1775, 1777 and 1778, 1780; in London 1749, 1751, 1755, 1767, 1795; in Salzburg Aberle saw 9 epidemics in thirty years—namely in 1816 and 1817, 1822, 1824 and 1825, 1828, 1831 and 1832, 1834 and 1835, 1836, 1840, 1844 and 1845; in Frankfort Speiss reported whooping-cough as recurring every three years.

To-day we find an annual endemic recurrence in all known regions, with exacerbations both in morbidity and mortality, every three or four years.

SYMPTOMATOLOGY.

IN the clinical picture of whooping-cough the paroxysm of cough stands out so conspicuously that it is not surprising to find it the characteristic from which the disease received its name.

The designations "tussis quintana" (Ballonius), "pertussis" (Sydenham, Huxham, Cullen), "tussis convulsiva" (Willis, Ettmüller, Sydenham), "tussis ferina" (Stoll, Sauvages), "tussis clamosa" (Kämpf), "tussis clangosa" (Bourdelin, Hasler), "Keichhusten" (Hufeland, Löbenstein-Löbel), "Eselshusten" (Jahn), "tosse canina" (Burserius), are, inasmuch as they are taken from the most striking symptom, all confirmatory of the teaching of Antonius Plaz, that tussis infantum is a species by itself, "quæ utplurimum magis morbum quam symptoma morbi constituit."

Moreover, the early observers found in its clinical course other important symptoms:

Whooping-cough attacks by preference children: "Tussis quinta pueros comprimis infestans" (Dovinetus), "Tussis infantum" (Mercatus), "Tussis infantum convulsiva" (Sydenham), "Architoux des enfans" (Hecquet).

Whooping-cough occurs epidemically: "Tussis epidemica infantum convulsiva" (Hoffmann).

Whooping-cough continues for a long time: "Tussis perennis" (Hasler).

Whooping-cough is pernicious to children: "Tussis infanticida" (Brüning).

Individual striking symptoms associated with the paroxysm were emphasized by some writers: On account of the accompanying cyanosis it was called "the blue cough"; on account of the suffocative symptoms, "the choke cough" (Holdefreund, Paldamus); on account of the general spasm, "tussis convulsiva" (Willis) or "catarrhe convulsif" (Laennec). The vomiting at the height of the paroxysm, which had been emphasized by de Baillou, induced the names "tussis stomachica convulsiva" (Kämpf), "tussis stomachalis" (Brouzet, Waldschmidt).

In later designations the writers attempted to give the nosography and pathogenesis of the disease as "bronchitis epidemica" (Marcus), "bronchitis convulsiva" (Fourcade-Prunet), "bronchocephalitis" (Desruelles), etc., names which fortunately disappeared with their origin.

The popular names for the disease in the different languages and countries are the most applicable, since they presuppose nothing. In Germany the current names are "Stickhusten," "Keuchhusten," "Schreihusten," "Blauer Husten," "Eselshusten"; in Switzerland, "Rehhusten"; in England since Willis, Sydenham, and Butter, "whooping-cough" and "kink-cough" (or "chin-cough"); in France, besides "coqueluche," "toux quinteuse," "toux bleu"; in Sweden, "Kichhosta," "Kramphosta," "Hopphosta"; in Italy, "tosse canina," "tosse ferina"; in Holland, "Kindhoest" and "Kwinthoest."

It has already been mentioned that the original signification of many

of these names was other than whooping-cough; for instance, coqueluche was primarily used to indicate influenza or la grippe, and only since the middle of the eighteenth century has it been employed in its present meaning, and Kindhoest was applied by Lævinus Lemnius to croup, and only gradually became synonymous with Kwindthoest, which Tricht invented for tussis quinta.

The most complete and shortest description of the disease was given by Cullen: "Morbus contagiosus; tussis convulsiva strangulans cum inspiratione sonora iterata, sæpe vomitus."

Since we will endeavor to extend this short description so as to cover a complete clinical picture, we will not go beyond the reports of those writers who have dealt with the severest epidemics, and our personal experience so far as it applies to frank cases.

A period of incubation varying from two to five to eight days in length without symptoms precedes the actual disease.

The first symptoms indicating the commencement of the prodromal or catarrhal stage are snuffles, headache, sneezing, watering of the eyes, a dry cough, and a feeling of constriction about the chest. This stage is called catarrhal on account of the similarity of its course to an ordinary catarrh of the respiratory passages. Occasionally it escapes the notice of the patient and his friends by the insignificance or short duration of the symptoms. According to careful observers, it lasts generally from three to eight or even fourteen days, though in severe epidemics the time may be decidedly shortened. In an outspoken catarrhal stage it is not rare to see an evening rise of temperature introduced by horripilation and followed by sweating. This fever, beginning on the third or fourth day, may last eight to ten days, is of an intermittent or remittent type, and terminates in uncomplicated cases shortly before the setting-in of the following stage.

Frequently the prodromal stage begins like an eruptive fever before the exanthem with exhaustion, rheumatic pains in the legs, headache, photophobia associated with a simple laryngotracheal catarrh, and anginoid pains. In this case it is more acute, lasts three to five days, and is characterized by a singular periodicity of the paroxysms, that to an attentive observer frequently indicates the diagnosis, even when a defluxion from the nose and injection of the conjunctiva would encourage the belief that the catarrhal, whoopy or dry, short cough, often accompanied by sneezing, was dependent on a simple catarrh.

Likewise toward the end of the prodromal stage the cough can in some cases be at once distinguished from that of a simple catarrh by the duration of the paroxysm and its occurrence at long intervals. Usually, however, it can be diagnosticated from an ordinary laryngeal

cough, or one due to an inflammation of the respiratory passages lower down, only by the increasing violence of the paroxysm associated with running from the nose, mouth, and eyes, and with a vomiting of food mixed with tenacious mucus.

Toward the end of a protracted catarrhal stage the cough assumes its peculiar spasmodic character, though in a very mild form. It begins with a tickling sensation in the throat or chest, it is dry, clear, and sharp. The children at once avoid all violent efforts,—running, speaking, the ascent of stairs,—because they come to realize that by them the attack will be brought on, lengthened, or made more painful.

Usually at this time the digestive tract is undisturbed. The appetite is good, digestion not influenced, and the bowel movements are regular. Only with high fever do we find a reaction of the stomach and bowels.

In severe epidemics the children complain of languor, heaviness of the legs, and mental dulness. In general, however, they are not disturbed in their little employments and games by the attacks.

With the transition of the simple cough into the intermittent paroxysms with whistling inspiration and expectoration of mucus begins the spasmodic or convulsive stage (*stadium spasmodicum s. convulsivum*). The boundary between this and the catarrhal stage already spoken of is frequently somewhat arbitrary, yet in more acute cases it may be very definite. It usually happens, after the cough has become more and more violent and terrifying for a few nights, that suddenly, usually at night, the first typical paroxysm with symptoms of suffocation and vomiting appears. And from this time on it is repeated at more or less regular intervals several times during the day and more frequently at night.

In normal cases fever ceases with the setting-in of the spasmodic stage. The associated symptoms and effects of the fever, and likewise the inflammation of the mucous membranes, rapidly disappear, and except for the actual paroxysms the patient seems in possession of complete health until the constantly recurring attacks produce greater or less disturbances, which we will discuss later. Hence in one sense the convulsive stage might be looked on as a sequel of the catarrhal stage.

The average duration of the spasmodic stage is about six weeks; it often lasts two or three months, and even half a year or longer, but never less than fourteen days. Normally, it runs its course without elevation of temperature.

The outspoken paroxysm that is characteristic of this stage may be

described in an uncomplicated case as follows: In the midst of his happy play the child feels the warning coming on. He becomes quiet, remains motionless, and holds his breath. If intelligent enough to explain his feelings, he describes a tickling sensation in the larynx or an irritation in the chest inclining him toward cough, or a tormenting constriction in the cardiac region. Other children and adults experience a tingling sensation ascending from the legs to the chest, or of dizziness or of considerable anxiety, with the impulse to run away. On the appearance of this aura the patient makes for some firm support,—a wall, a bedside, a curtain, or his mother's knees,—or he seizes hold of the person nearest him.

The sensations preceding the attack may last a minute or even a quarter of an hour. They are often associated with yawning or sneezing. Finally, with the patient in the greatest state of perturbation, the explosion of cough takes place.

An intermittent expiration, broken into shrill, impulsive shocks, 3 to 10 or more following one another, continued to the limit of breathlessness, then a short, rapid, and deep inspiration associated with a high whistling, sipping, or crowing sound, the whole repeated several times until finally, under threatening asphyxia, the paroxysm terminates with the expulsion of a scanty or considerable amount of tenacious white secretion and the vomiting of mucus and food. There may be an interval of one or several minutes between the expiratory discharge and the spasmodic attempts at inspiration, producing, under increasing cyanosis of the face and neck, and with inordinate protrusion of the spoon-shaped tongue from the convulsively opened mouth, a picture of imminent suffocation.

The stormy action of the respiratory muscles preceding the asphyxia is evident during expiration from the violent trembling of the belly-wall, and during inspiration from the marked contraction of the abdominal muscles, bulging of the larynx, and tension of the muscles of the neck, and it is accompanied by general muscular spasm throughout the body. The protrusion forward of the lower part of the trunk changes with every sudden tension and relaxation of the body. Children stamp their little feet with every effort, and during the asphyxia convulsive tremors pass over their extremities and face.

At the height of the attack the countenance exhibits the staring expression of an epileptic; it becomes cyanosed, swollen, the eyes bulge forward, the sclera is injected, the neck expands, the facial and cervical veins stand out and beat violently, froth gushes from the mouth and nose, occasionally mixed with blood, a stream of tears

pours over the cheeks, and sometimes a hemorrhage appears from the ears. The sphincters may relax unconsciously. If passed during the attack the urine is copious, pale, and of light specific gravity; otherwise it is concentrated and clouded with urates.

The severe suffocative symptoms become more threatening, the seldomer expiration follows; the crisis with the expulsion of mucus and vomiting follows more quickly and easily the more violent and frequent the jerking cough becomes. The crisis in severe paroxysms is usually succeeded by a longer or shorter period of stupor. Then after some seconds or minutes the return to consciousness occurs, with convulsions which are occasionally violent, eructations, vomiting, strangling, singultus, or sneezing. The respirations after an attack are for some time shallow, short, and anxious. Languor, prostration, a fit of crying, or drowsiness closes the scene.

Although after a mild paroxysm children return again in haste to their play as if nothing had happened, after the severest ones they often lie for a long time in the prostration of a swoon, pulseless and breathing superficially; from this condition the restoration of strength and consciousness is very gradual.

At the beginning and close of the spasmodic stage the paroxysms are usually mild and short, running their course in half a minute or a few minutes, with several impulsive coughs followed by a long whistling stridor. At the height of the disease they are longer and more frequent, so that often 10, 15, 20, crowing inspirations may be counted between the expiratory discharges. The whole scene may be drawn out for a quarter of an hour in an uninterrupted change between the series of jerking expiratory explosions, 10 to 15 at a time, and the interpolated crowing inspirations until the ejection of tough mucus brings it to an end. Nor is this all, for not rarely after a short pause the curtain rises to repeat again once or even twice the same scene.

During the night and toward morning the attacks are usually very violent. The child wakes from a sleep that has become gradually restless with a nameless dread, a feeling of suffocation, a livid countenance, in a cold sweat, till by an extra effort he catches his breath in a long loud whistle, only to be immediately carried back again into the midst of a paroxysm. There are rare cases where every attempt on the part of the child to lie down is met with a new seizure. Nay more, we have watched by the bedside of a child prostrated by the duration of the disease where every time the eyes closed and the tired head sank backward, a furious paroxysm seized it, so that an actual convulsive state existed for hours, or indeed even until daybreak.

Every attack may be accompanied by sneezing, as well as by vomiting, or terminate with it.   Josef Franck reported a case where the child sneezed fifteen times during every paroxysm, and in the notes of his father, Johann Peter, he found the record of a little countess who sneezed more than one hundred times.   According to different writers, the entire paroxysm of coughing may be replaced by a long-continued explosion of sneezes.

The congestion of the upper portion of the body during an attack frequently results in ecchymoses between the conjunctiva and sclera, and in the skin of the face and neck.   The tension of the muscles and the violent body movements during the convulsive seizure leave behind them pains in the chest, abdomen, and extremities.   Most commonly after the paroxysm there is an interval of complete comfort.

We have already mentioned that, apart from the attack, there are normally no symptoms.   Sometimes the laryngoscope shows laryngeal or tracheal inflammation, but we must agree with Rossbach that this is not the rule, as many authors assert.   Slight rises of temperature after severe attacks frequently pass unnoticed, though they can be shown by the thermometer.   High temperatures, as also gastric disturbances, indicate complications.   Not infrequently the sleep is restless.   In this case the child lies with half-open eyes, moaning quietly but anxiously, till the appearance of the attack.   Enlargement of the spleen, absent in simple cases, may be present with complications off and on, though, remarkable to say, no writer mentions it.

The free interval is, corresponding to the number and duration of the attacks, of varying length, and refreshing.   According to the character of the convulsive stage, the age and strength of the child, the severity of the epidemic, the paroxysm may repeat itself in twenty-four hours from five to fifty times, and, depending on the patient, a good or no recovery may result.   In mild cases there is between the seizures such a complete feeling of well-being that the child plays lustily, eats with good appetite, sleeps, except at the time of the attacks, without disturbance, and scarcely loses at any time a healthy appearance. When the disease is of long duration and the attacks follow one another rapidly day and night, the patient falls away, loses strength, and develops edema of the face and sometimes of the extremities.   Loss of appetite increases the wasting or voracity leads to excesses in eating which disturb digestion and assimilation, and everything augments the attack.

In isolated earlier epidemics there was reported, at the height of the disease, diarrhea with tenesmus, or dysentery, vesicular and purpuric

eruptions on the body, even pemphigus and furunculosis (Jadelot), accompanied by marasmus in which the patient tossed about anxiously or unconsciously, whimpered constantly, and refused food and drink until, emaciated and wasted by the mucous evacuations, death took place in a general convulsion.

The expulsion of round worms by the mouth or anus signified, according to the old writers, the last degree of exhaustion, as the flight of rats from a ship foretells its going down (L. Lemnius).

In the present-day epidemics not all the severe terminations of the convulsive stage have been observed. Usually after three to four weeks fastigium, accompanied by increasing vigor, the free intervals become longer and the paroxysms shorter. Even in the severest cases the *stadium decrementi* delays but little longer. The beginning of this last may be assumed when there is a progressive decrease in the violence and frequency of the spasms, when the whistling inspiration becomes less noticeable, and cyanosis, at the height of the attack, is less pronounced.

The jerking expirations continue into the stage of convalescence, but the attacks appear now only at night or after heavy meals, or rapid drinking, or on laughing or crying. The intervals between them are irregular, and no restlessness or anxiety announces them. They no longer threaten suffocation and they terminate less frequently with vomiting. The patient, worn out during the convulsive stage by the muscular efforts, by the disturbance of assimilation, and by loss of sleep, gains gradually in weight and strength. His old liveliness returns. His appetite, which varied between indifference and voracity, becomes normal.

Finally, only extraordinary influences are capable of again exciting the old fits of coughing. Unfavorable changes of weather, gross dietetic errors, unusual efforts, intense emotional excitement, may now and again provoke a paroxysm. Blache saw two children, after seeming recovery for a month, fall into a violent paroxysm from rage.

The last stage may continue from a few days to many months. The more wide-spread the plague, the more rapid its course and that of the spasmodic stage. The cases of longest duration are observed in the mild, sluggish epidemics. The stadium decrementi is the most dangerous as far as life is concerned. The patient rarely succumbs to the attacks during the fastigium, and during this period serious complications are uncommon, but with the transition of the paroxysms into the last stage the complications and sequelæ show themselves in their full severity. But of these later.

The duration of the whole disease in severe epidemics, as observed by Friedrich Jahn, Whithead, and others, is four, six, eight, twelve weeks. Judging by chance remarks, the course in the first epidemics of Ballonius, Mercatus, and Sydenham must have been much more acute. A duration of from ten to twelve weeks must be taken as the minimum for severe cases in epidemics occurring in large cities. A duration of six months is not uncommon, especially for cases that begin in autumn, and the extension of the disease over a whole year has been now and then observed by the most experienced physicians.

According to the estimates of West, Rilliet and Barthez, and Trousseau, the average duration is from seven to ten weeks. While Matthaei at the beginning of the nineteenth century never saw the convulsive stage last over from four to six weeks, Jacobi reported several cases during the epidemic at Vaals near Aix-la-Chapelle in 1797 and 1798 with a duration of from sixteen to twenty weeks.

There is no doubt that a decided shortening of the disease may be produced by a change in the weather. Many writers confirm this, particularly Jahn, whose veracity is unquestionable; and William Heberden hesitates not to say: "mutationem cœli maxime valere ad vim morbi leniendam et finem ejus accelerandum."

The duration is likewise decidedly influenced by treatment. But we will discuss later on the specific drugs and methods which, according to every sanguine therapeutist, are capable of limiting the course of the disease to four, three, or even two weeks. We might mention here that Trousseau reports a case that lasted only three days. If this minimum is compared with the maximal duration continuing throughout a year, the limits, Biermer remarks, are wide enough to prevent surprise at any course the disease may take.

For those who like a graphic scheme, in spite of the fact that circumstances may occasion many alterations, we introduce the following as a time proportioned for the different stages.

I. Incubation	1	week	(2– 8 days)
II. Incrementum	1–2	weeks	(3– 40 days)
III. Fastigium	4–6	"	(30–140 days)
IV. Decrementum	3	"	(20–300 days)

As a general remark, the frequently repeated observation of different writers (Jahn and others) must be mentioned—namely, that the more severe the epidemic, the more inflammatory complications occur with it, and the more the personal constitution is predisposed to inflammations, the shorter are the second and third stages.

As to the *course of whooping-cough in individual cases,* every physi-

cian has had the experience of seeing different cases in the same family or the same house run quite different courses and last for very different periods of time.

That abortive cases of whooping-cough occur, is proved by Trousseau's case.

The symptomatology may vary through every degree and form of development. The most striking characteristics of the disease may be obliterated. The stridor itself may be absent, especially in sucklings.

With the appearance of an inflammatory disease, an outspoken case may very soon change so as to be unrecognizable. Cullen, Burns, and Watt report instances where the stridor immediately vanished on the breaking-out of an inflammation of the lungs or of a brain disease. According to Lacroisade, the appearance of diphtheria or of an eruptive fever is the signal for the cessation, or at least the decrease, of the symptoms. It very rarely happens, as in one case of complicating measles, that the paroxysms increase in severity. Michael Ettmüller reported an epidemic at Jüterbogk in 1804, in which, after an inoculation with vaccinia, the paroxysms entirely disappeared with the coming-on of the fever on the seventh or eighth day, "without any particular medication."

All these experiences are made known by Hippocrates in his "Prognostics" in the aphorism: "Spasmos febris superveniens acuta solvit."

The number of paroxysms in the twenty-four hours, as mentioned before, varies considerably according to the stage of the disease, the intensity of the virus, and the constitution of the patient. The attack occurs spontaneously at least two or three times daily, no matter how carefully the patient may avoid exciting influences.

Some of the extraneous causes that go to increase the number of paroxysms are: eating and drinking too much or too rapidly, especially the overloading of the stomach with solid food (just as, in fact, the cough in an ordinary cold may be seen to increase after meals); violent respiratory movements, as in laughing, crying, sneezing, yawning; uncommonly violent bodily efforts, as in jumping, running; irritation of the skin, especially by drafts or the touching of cold objects; titillation of the nasal mucous membrane, as by smoke, or even a strong odor; psychic excitement, as fright, anger, rage, to which children spoiled during the disease by complaisant parents are very liable.

Like yawning, the paroxysm of whooping-cough is undoubtedly excited by mimicry, for let one child begin, and all in his immediate

neighborhood will follow, even if, as Meltzer has noticed, the children happen to be in a separate room and merely hear the cough.

A decrease in the number of seizures, as a result of external influences, has been observed. Change of air, the transference to another climate, often effect this. Their severity is unquestionably influenced by changes of weather.

Friedrich Jahn recounts, in his observing way: "June was beautiful, dry and warm; the majority of 'whooping' children paid little attention to their cough. Everywhere the children ran about lustily, and when an attack came on, they coughed their cough vigorously. They withdrew a little from the crowd, supported themselves against some object, and when the paroxysm was over they re-entered into the play with the same spirit and pleasure as previously. The fits themselves were shorter, milder, and less frequent.

"But at the end of June, and throughout almost the entire month of July, the weather was wet and cold. A heavy hail-storm lowered the general temperature considerably. Simultaneously with, and immediately after, this change the paroxysms became more violent, the children lost all interest in play, fever set in or increased, and in cases where the cough was declining, it began anew.

"The warmth and dryness of August came again to the aid of the treatment, and improved the general condition."

It has been observed that threatening attacks were suppressed by fear, anxiety, fright, and even by the diverting of attention from them. Some physicians go so far as to reckon fright or shock among the remedies for the disease. The first of these was Willis; the last, Felix Niemeyer.

According to Matthaei's observations, induced emesis causes the next four or five attacks to lose much of their violence, but then they return with their original vigor. Holdefreund's assertion that the seizure is milder after a discharge of wind, either by the mouth or the anus, has been confirmed by others.

According to many writers, the varying numbers of paroxysms correspond to definite types induced by a certain *genius epidemicus*, like intermittent fever, and they are accompanied by typical temperature curves.

Aaskow observed a "typus quotidianus duplex" in a Copenhagen epidemic in 1767, and Ozanam the same at Milan in 1815.

Rosenstein reported a "typus tertianus" in 1755 in Sweden, Mellin (1768–1769) in Langensalza, William Butter (1733) in Derby, Stoll (1781) in Vienna, Hufeland (1786) in Weimar, Jahn (1805) in Meiningen, Winogradow (1823) in Moscow. Jacques Mellin reported a "typus tertianus duplex" in a few cases in 1769.

A. Götz observed a whooping-cough epidemic in southern Russia in 1866 that ran the course of febris intermittens. At the acme of the disease he employed successfully quinin sulphate.

The *termination* of whooping-cough, when no complications interfere, is usually in complete recovery, though through a longer or shorter stage of convalescence. Rarely does a violent attack cause death by asphyxia or syncope, and a fatality in the convulsive stage through marasmus or a lingering fever is rare. It is uncommon, too, for patients to succumb to gradual sapping of the vitality in cases of severe inanition and continued loss of sleep.

Now and then deaths are reported from complications during the attack, as cerebral apoplexy, profuse external hemorrhage, and emphysema of the subcutaneous tissues after rupture of the larynx. But death occurs most frequently from a complicating pneumonia inducing heart failure, or a bronchitis ending in suffocation.

A fatal secondary dropsy has been observed in isolated epidemics, as may be found in the communications of Rosén von Rosenstein in Sweden, and likewise Lombard in relation to the Geneva epidemic of 1838.

A termination in partial recovery is not infrequent. There may remain severe disturbances of the nervous system, weakness of intellect and memory, imbecility, hemiplegia with posthemiplegic chorea, epilepsy, visual defects, even to blindness, deafness, deaf-muteness; injuries to the respiratory apparatus, emphysema, chronic catarrh, predisposition to laryngismus stridulus, to asthmatic attacks, tuberculosis; cardiac weakness; even curvature of the spinal column as a result of dislocation of vertebræ, and deformities of the thorax from badly treated fracture of the ribs.

COMPLICATIONS.

THE normal course of whooping-cough, in many cases and in some epidemics, is in almost all cases altered by coincident diseases or its severity is increased by special circumstances.

It is not yet possible to decide in regard to all these complications whether they are merely the direct or the indirect results of the virus of the disease, and therefore should be regarded as symptoms, or whether they are secondary affections, and therefore combinations with the whooping-cough.

There are, without doubt, a whole series of catarrhal inflammations that are to be looked on as symptoms which usually appear in the pro-dromal and may extend over into the nervous stage, as laryngitis and tracheitis, bronchitis, and even pulmonary inflammations. These last have been observed in particularly pernicious epidemics, and in rachitic and scrofulous children, though occasionally in ordinary epidemics also.

These inflammatory complications have been met with more rarely in recent epidemics than in earlier ones. But the investigation of the latter has produced the indubitable impression that whooping-cough has lessened in severity from century to century as much as it has gained in duration and obstinacy. It has taught, in addition, that the mortality of the early epidemics was mostly due to the violent inflammatory processes that took place in the upper air-passages at the beginning of the disease. The intense dyspnea and high mortality through suffocation in de Baillou's epidemic of 1578 can be understood only on the assumption of a very acute laryngitis, with inflammatory edema or a spasm of the glottis.

And yet possibly Ballonius failed to differentiate between individual cases of laryngitis and pertussis. For that both may occur epidemically at the same time is well known, and Wahlbom has expressly reported an "angina suffocatoria epidemica" preceding an epidemic of whooping-cough on the island of Oeland in 1763.

In our day a simple mild laryngitis and catarrhal bronchitis in the first stage are reckoned as common symptoms of the disease. They may continue through the second stage, and are then usually not accompanied by fever as long as the catarrh is limited to the larger bronchi. But with the extension of the inflammation to the medium tubes and bronchioles, acute general symptoms with rise of temperature and dyspnea make their appearance.

A secondary inflammation of the larynx, trachea, bronchi, or lungs
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during the spasmodic stage is always to be regarded as an extraneous combination. And this may come on at any time, though more frequently toward the end than at the beginning or acme of the convulsive stage.

The setting in of a *bronchitis* and *bronchiolitis* in this stage is characterized by flushing of the face, a hot skin, lively thirst, loss of appetite, and rise of temperature. The respiration in children may increase to 30, 40, or 50, the pulse to from 120 to 150, and the temperature to 38°, 39°, or 40° C. The respiratory murmurs are unequal and irregular, and the breathing is sighing. The breathing becomes abdominal, and is accompanied by movements of the alæ nasi. Fine moist or subcrepitant râles are heard over the lower portions of the lungs. The child gradually succumbs to symptoms of suffocation, and death occurs usually in a few days under marked cyanosis and swelling of the face or increasing pallor.

Simple *congestion of the lungs* of one day's duration with fever and slight dulness over the whole chest has been reported by different writers since Laennec.

Bronchopneumonia, the most frequent and severest complication, comes on in the convulsive stage, rarely in the prodromal stage or during convalescence. In some epidemics it occasions a frightful mortality. Roger and Cadet saw it in every fifth case, and Lacroisade reported 22 deaths from it in 103 children treated in the Hôpital des Enfants de Sainte Eugénie. See found it occurring in every third child. It generally sets in during the second or third week of the spasmodic stage, attacks by preference children between two and five years of age, and is more frequent and more dangerous the younger the child. It is almost absolutely fatal to children under three.

Bronchopneumonia but seldom breaks out suddenly, and then its course is marked by a continued fever; its beginning is generally insidious and progressive. Evening rise of temperature, general weakness, prostration, and dyspnea are its characteristic symptoms. The paroxysms of cough lessen in intensity. The skin is at first hot and moist, but as the fever increases it becomes dry. Temperatures from 38° to 39° C. are common, from 40° to 41° C. and over are not rare. The full, quick pulse may reach 130 to 160 or even 200. Thirty, forty, and up to eighty hurried, fatiguing respirations proclaim the increasing consolidation of the lung tissue. Vomiting and diarrhea are soon added. There is a tormenting cough with profuse expectoration at first of white, frothy mucus, which later becomes reddish and tenacious.

Usually, as mentioned before, the peculiar whooping attacks diminish in frequency and intensity during the pneumonia. Very rarely they increase in frequency so as to recur every fifteen minutes. Bergeron saw them continuing in spite of a pulse of 156, and a respiratory frequency of 75. These exceptions do not contradict the rule that pneumonia usually lessens the severity of the pertussis, so that in in the worst cases the attacks become atypical, lose their stridor, terminate without vomiting, and run their course with increasing dyspnea and pallor under continuous efforts of the auxiliary muscles of respiration, while in the most favorable cases the whole course of the pertussis is interrupted by the pneumonia, or even, as Trousseau asserts, cured. Joffroy looks upon the augmentation or diminution of the fits of whooping-cough as an indication of the amelioration or aggravation of the pneumonia.

A fatal termination of pertussis pneumonia is almost certain in young children. After several alternate swingings toward better and worse, death occurs on the fourth or fifth day, seldom at the beginning, usually with a marked rise of temperature, even to 41° C.; extreme dyspnea, with stertor; a rapid, weak heart action, 200 to 210 per minute; and increasing obstruction of the bronchi with mucus, resulting in suffocation.

Recovery occurs in only 4% to 5% of the cases, with gradual reduction of the inflammatory symptoms, disappearance of the prostration, and return of appetite.

Lobar pneumonia as a complication of whooping-cough is much rarer than bronchopneumonia. When it appears, it is in the usual form, but, as the cases reported by Rilliet and Barthez, and Lacroisade and myself, teach us, attacking by preference the upper lobes, and being less dangerous than bronchopneumonia. Diminution or disappearance of the attacks of coughing is the rule.

Pleuritis exsudativa with effusion is a rare and serious complication occurring in older children and adults. In small children it has not been observed.

Pericarditis and *endocarditis* are mentioned as rare accidents by Guibert.

Simple *meningitis* of non-tubercular origin has been spoken of now and then, but without authority.

The most common nervous complication is spasm of the glottis ("convulsions internes" of the French physicians). It is seen especially in nervous and scrofulous individuals, and even in the mildest cases may cause death (Lancisi, Blaud, Combes). According to the

inaugural thesis of Dr. du Castel, the first certain observation of this fatality was by William Hugues, in a nine months' old infant, with a postmortem finding of thymus hypertrophy. Spasm of the glottis scarcely ever occurs before the fourth year of life. It is to be feared when in the attack, instead of a sudden hissing inspiration a complete suppression of breathing, with cyanosis spreading over the entire body, follows the convulsive cough. In a condition of intense lividity, accompanied by swelling of the face, the child falls unconscious, and in convulsions, till at length a long whistling inspiration brings to an end the threatening suffocation.

These attacks occur particularly at night. The pulse in every subsequent seizure becomes more rapid and smaller. Profuse sweating takes place all over the body, and the child dies in a state of asphyxia. Or else after a series of paroxysms it succumbs to the repeated asphyxial attacks in a condition of increasing coma or in convulsions. According to du Castel, Rilliet, and Levrat, a fatal termination is the rule.

Eclamptic attacks ("convulsions externes") are not uncommon in children with an inclination to convulsions, or in those who manifest symptoms of hydrocephalus. They occur in mild forms of whooping-cough frequently during teething, yet also as late as the fifth year, and appear usually between the eighteenth and thirty-fifth day of the disease. According to some, they take place more frequently, the more violent are the coughing attacks. They are ushered in by excitement or its opposite, drowsiness, and often, again, with extreme dyspnea. They occur subsequent to a paroxysm of coughing, or they happen during a free interval or interrupt the seizure, thereby changing its character, or causing the paroxysms to cease entirely.

With the commencement of the convulsion, the thumbs are forcibly pressed on the palms, the hand is flexed, the big toe crooked, and irregular movements in the muscles of the eye follow. The pupils remain dilated, and the eyes look upward and inward. Extreme dyspnea gives way to profound coma, the stillness of which is interrupted only by the twitching in the limbs. Finally, a deep or several superficial inspirations, usually without stridor, announce the end and the return of consciousness, or a deep coma continues till the next attack.

The scene usually gains in violence with every repetition. In favorable cases, which are very rare, the subsequent fits become milder and milder, and the cough, the forcible expiration, and the terrifying inspiration cease. In others the convulsions that were only local in the beginning, become general, and the child sinks under the prostra-

tion, and dies within the first three days.   Among 10 children, 9 are certainly doomed.

Ordinarily, with the appearance of the eclampsia the child exhibits, instead of the swollen cyanosed countenance and distended neck, as in a paroxysm, pale bloodless features.   Subsequent paralyses or contractures point in isolated cases to more profound brain lesions as the cause or result of the paroxysm.

Möbius lately reported increasing paralysis, likewise hemiplegia and psychic disturbances following the disease.

Richter has blamed the misuse of narcotics for the ocular and other nervous disturbances, already mentioned—that is, amaurosis, amblyopia, loss of memory, epilepsy, etc.; while Gölis, Otto, Hufeland, and Jahn attribute them to congestion of the brain arising from the careless administration of belladonna.

As mechanical effects of the paroxysm, we may point to the following:

Hemorrhages into different parts of the skin and mucous membranes.   They originate, as in epilepsy, from violent attacks associated with flushing and swelling of the face, forcible beating of the carotids and the temporal arteries, and dilatation of the cervical veins.

The most common is more or less profuse *nasal hemorrhage.*   This usually continues only so far as to produce a comfortable feeling by reduction of the cerebral congestion, but it may become dangerous by frequency and excess, and may even prove fatal.   Serious hydremia has arisen from epistaxis, which resulted in a further inclination toward hemorrhage.   More frequent and serious attacks of nose-bleeding have been reported from spring and summer than from winter epidemics.

Total or partial *ecchymoses of the conjunctiva* are rare.   The total, inasmuch as they except only the cornea, disfigure the child frightfully and prevent movement of the eye.   The absorption of the blood takes from two to four weeks.

Ecchymoses of the eyelid are more frequent.   They may be one-sided or double-sided.   They disappear more rapidly than the hematoma of the conjunctiva when both occur together.

Conjunctival hemorrhages are very rare, but when they take place they may be mistaken for bloody tears by the mixing of lacrimal secretion with the blood.   The dripping of bloody tears has been reported by de Haen, Trousseau, Bouchut, and others.

Hemorrhages from the ear are mentioned by Wilde, of Dublin, Blache, Triquet, Gibb, and Roger.   In the accurately observed cases the source of the bleeding was the external auditory meatus or a rup-

tured tympanum; along with these sometimes an inflammation of the external ear showed itself, though sometimes no cause was discovered, so that the hemorrhage must be regarded as a purely mechanical epiphenomenon. The amount of blood poured out, on rupture of the tympanum, was in one case reported by Triquet as a teaspoonful, though usually it was much smaller.

Hemorrhages into the skin, as petechiæ and ecchymoses, occur mostly on the face and neck. Purpura on the neck, buttocks, and extremities has been reported in cachectic individuals. Hemorrhages from wounds, from lip and nasal fissures, and from ulcers have been frequently seen. Trousseau saw in a young woman small drops of blood flowing with every paroxysm from a nævus maternus over her left eye, and van Swieten saw a fatal hemorrhage follow rupture of a scar on the head.

Hemorrhages from the lips, gums, tongue, palate, tonsils, and pharynx are uncommon (Roger, Bouchut). Hemorrhages from the frenum of the tongue caused by lacerating it against the lower incisor teeth, or by biting it during the attack, are of more frequent occurrence. All these hemorrhages from the mouth are less important on account of their amount (they would scarcely fill a teaspoonful in twenty-four hours) than on account of the frequency with which they are confounded with hemoptysis and hematemesis.

In general, it may be stated, as Roger asserts, that hemoptysis in children under ten years of age is almost unheard of. Bouchut also denies consistently the occurrence of hemoptysis in the whooping-cough of children, while Asti reports fatal pulmonary hemorrhages. Quarin, Josef Franck, and Trousseau, speaking of bronchial hemorrhages, consider them not only not dangerous, but even favorable to the patient. They regard them of the same benefit as Sydenham regarded venesection in whooping-cough. Fernet declares that bronchial hemorrhage is rare.

Hematemesis, at most very rare in children, has been denied by the majority of writers, and when it does occur it is to be referred to the swallowing of blood from the pharynx.

Subpleural hemorrhages, or meningeal hemorrhage into the arachnoidal sac (Barrier), an intense hyperemia of the kidneys with hemorrhage into the suprarenal body (Roger), have been found incidentally postmortem.

Cerebral hemorrhages with paralyses, loss of memory, and amaurosis were first reported by Butter.

Menorrhagia and *abortion* are rare; at least Simpson, an expe-

rienced obstetrician, assures us he never saw them. According to Schott, Biermer records a case of rupture of the membranes of the ovum with hydrorrhea as the result of whooping-cough.

Anasarca of the face and neck has been reported by Rilliet and Barthez, and wide-spread dropsy by Rosén, Franck, and Lombard. Franck also mentions two cases of acute hydrocephalus in which, in place of constipation, there were frequent liquid evacuations.

Vomiting is so common as an accompaniment of whooping-cough that Kämpf, Brouzet, Waldschmidt, and others regard pertussis as primarily a stomach affection, and Chambon insisted that it was a special form of gastric catarrh. It usually occurs at the end of the attacks, seldom in the intervals. The vomit consists mainly of mucus, often mixed with food, either unchanged or digested, according to the length of time it has been in the stomach.

When in certain cases food that has been in the stomach for hours appears entirely undigested, it is to be referred to a participation of the stomach in the disease, though nothing more accurate is known about it. As a rule, the vomiting may be looked on as a mechanical result of the coughing explosions. That in individual epidemics it may be a neurosis analogous to the whooping paroxysms is partly evidenced by the cases where an actual hyperemesis must be combated.

Unconscious passage of urine and feces, prolapses of the anus and uterus, the origin of goiter, aneurysms, inguinal and umbilical ruptures, strangulation of herniæ previously existing, fractures of the ribs (Gooch), dislocations and fractures of vertebræ (Friedrich Hoffmann, Richter), have been recorded as further mechanical results.

Rupture of the tympanum has already been mentioned under hemorrhages from the ear. It takes place near the malleolar process, or at the periphery; it may be linear or transverse, single or multiple, unilateral or bilateral. Gibb saw this complication four times in 2000 cases. Triquet reports two observations of it.

A very frequent, in fact, almost regular, complication of whooping-cough is a *laceration of the frenum of the tongue.* It may be a cross-tear, or appear as an oval ulcer.

Amelung was the first to describe it as occurring in more than half of the cases during the convulsive stage. Considerable discussion took place concerning this phenomenon, in which Braun, Brück, Zitterland, Gamberini, Bouchut, and others took part with zeal, and even the Parisian Académie has long shared in it. After Zitterland had described the phenomenon as a vesicle, Lerch as an ulcerated pustule, Delthil and de Nogent as the manifestation of a specific disease analogous to the hard chancre of syphilis, or the lyssa of hydrophobia, Gamberini,

Schmidt, Bouchut, and Roger broke the back of the evidence by demonstrating that it was nothing more than a simple laceration on the under border of the tongue, due to the mechanical effect of forcible protrusion during a paroxysm. As a matter of fact, this laceration is seen only in the spasmodic stage, most commonly in children with sharp teeth, seldom in adults with blunt ones, and almost never before the cutting of the incisor teeth. It has been noticed that when the ulcer is in an uncommon situation, the curve of the teeth or the shape of the tongue itself is peculiar. And when Delthil, in opposition to this opinion, brought forward two cases in which the laceration arose before dentition, Bouffiers reported several such cases, but explained them in this manner: that the mother in forcibly removing the mucus from the mouth of the child, probably injured the frenum.

The course of the ulcer formation is as follows: At the beginning a bright redness is seen on the free margin of the frenum, succeeded by an erosion of the mucous membrane, or a linear tear or a little papule of grayish-white or mother-of-pearl-like glistening color with a breadth of 2 to 3 mm. This soon, in turn, becomes a small oval ulcer with irregular, slightly elevated border, and a whitish or grayish floor.

The lesion remains limited to the frenum, or extends more or less deeply and on both sides into the under surface of the tongue, when it forms a broad ulcer covered by a grayish deposit, as seen in aphthæ or in the cheek ulcers produced by sharp teeth.

It is very uncommon to find the ulcer on the side of the frenum or on the upper surface of the tongue. It is uncommon to find swelling of the submaxillary glands.

With the abatement of the paroxysms of cough, healing gradually takes place with or without scar-formation. There is no likelihood of a cicatrix, when present, producing any disturbance of movement in the tongue.

In reference to pulmonary emphysema as a result of whooping-cough, the independent authorities are quite at variance. For while Trousseau and Jaccoud mention it as arising in the cough paroxysms, Rilliet and Barthez insist that not only is this impossible, but that an existing emphysema may be cured by whooping-cough.

Postmortem, all forms of emphysema have been found in children succumbing to the disease, both the vesicular with distended vesicles on the surface of the lung, especially in the apices and margins of the lungs and around consolidated areas, and also the interlobular, in which isolated or numerous lobules may be torn, resulting in the presence of air in the interstitial substance, or subpleural emphysema, or even *general cutaneous emphysema*. In this last case Guillot, Blache, and Roger found the pleura detached even to the root of the lung,

whence the air forced its way along the great vessels to the neck, face, chest, and entire body. General emphysema has also been observed as a result of laceration of the larynx during a paroxysm. It usually leads to death.

Rilliet and Barthez saw acute *bronchiectasis* most commonly in children from three to five years of age, which proved fatal in three or four days. Laennec attributed its origin to whooping-cough alone, but others contend that a bronchopneumonia is necessary. Rilliet and Barthez, Hardy and Behier, make the obstruction of the bronchus by mucus the cause, in that they assert that the coughing forces the mucus backward into the bronchi, dilating them. Others believe the process to occur from aspiration of air beneath the mucous membrane, where it is warmed, and then produces a distention of the elastic tissue. Stokes, Trojanowski, and Charcot attribute it to inflammatory paralysis or disturbance of the muscles of Reisessen, etc. The condition usually disappears, seldom becoming chronic.

Chronic catarrh of the stomach or intestine as a complication or sequel is infrequent. When it appears, it is always dependent on other digestive disturbances. Some of the older writers describe it as an everyday accompaniment of whooping-cough, but it is impossible to shut out the suspicion that lack of consideration for the digestive tract in the treatment by emetics, narcotics, expectorants, etc., was more to blame than the disease.

The first *sequela* of whooping-cough to be mentioned is whooping-cough itself, or at least a cough sounding like it that not rarely appears during the winter, even after complete recovery. Trousseau insisted that this was mostly a psychic (hysteric) imitation of pertussis: "Le malade tousse, car l'organisme se souvient des habitudes d'autrefois."

There may be some difficulty in differentiating this "toux coqueluchoide" from a true secondary infection with whooping-cough; but this latter, according to all authorities, constitutes a most rare exception. Rosén von Rosenstein in thirty-eight years saw no second attack; Ozanam reported but two cases; Trousseau, two; Gibb, two; West, one.

Temporary interruptions of the disease and a resumed course after weeks or months, so that, for instance, the attack appears in spring, gives no manifestation in summer, and recurs in the autumn, have been reported by West, Copeland, and others. Morris, who saw similar occurrences in several children, aptly compares this phenomenon to the recurrence of intermittent fever attacks.

Among extraneous diseases occurring frequently in the last stage,

or following immediately after, must be mentioned *tuberculosis* and *rachitis*. Although it is often true that the inauguration of these diseases occurred even before the whooping-cough, and were incited by this only to a more rapid course or further extension, there is no doubt that previously strong, healthy children present gradually or quickly developing symptoms as a result of pertussis.

A rachitic sternum, chicken-breast, distorted spinal column, are not infrequent consequences of the disease, yet we have no grounds for attributing the hunchback condition to whooping-cough as the direct cause. Pulmonary phthisis, which used to be thought a special form or termination of pertussis, has been considered since Trousseau's time as an accidental infection for which whooping-cough paved the way. It usually develops in the stadium decrementi, most commonly in the case of older children, and is to be feared between the ages of six and ten, when the cough continues in a short dry form, associated with emaciation, evening rise of temperature, and night sweats.

Besides chronic pulmonary tuberculosis, which is the most frequent form of tuberculosis, acute galloping consumption (tubercular pneumonia) is rarely seen; sometimes general miliary tuberculosis is met with.

Tubercular meningitis, with its ordinary malignant course, has been observed in the last stage of pertussis by Ch. West, and Rilliet and Barthez.

In general, the course of whooping-cough becomes more unfavorable, and the danger to life is increased by every severe complication or combination. The reverse is also true, that pertussis aggravates the prognosis of any previously existing disease, as, for instance, tuberculosis and phthisis. Schönlein has drawn attention to its remarkable influence in an epidemic form on phthisical patients. According to him, during a pertussis epidemic the vascular and febrile symptoms of consumption disappear, and the cough takes on a periodic character and becomes more violent. At least this occurs in the majority of cases.

It is still a matter of discussion as to whether pertussis has any favorable or unfavorable influence on other epidemic diseases. The relation between whooping-cough and measles, which is somewhat similar to that between diphtheria and scarlet fever, is well known. Pertussis seldom precedes, yet often follows, measles. In 495 epidemics collected by Hirsch, pertussis was combined with measles in 58, preceded it in 11, and followed it in 25. In certain epidemics the relations between the two were so close that some writers insisted on

their identity.   We shall speak more fully about this later, yet we may say here that whenever measles occurs with pertussis, the general condition of the patient is made worse, the spasmodic attacks become milder, during the course of the eruptive fever.   All experience goes to show that the combination of the two increases the susceptibility to chest affections, especially tuberculosis.

How scarlet fever acts on a pertussis epidemic has not been determined.   Ettmüller saw whooping-cough follow a scarlet fever epidemic, but the patients who suffered from the former were not attacked by the latter.   Watt reports the interruption of a pertussis epidemic in an outbreak of scarlet fever.   According to Danz, scarlet fever and measles and whooping-cough may occur simultaneously in the same individuals without one disease interfering with the other. The same has been reported by Hufeland from an epidemic at Weimar in 1786.

Hufeland and Lentin believed that children suffering from favus, scabies, and chronic eczema were more immune to pertussis than others; Jahn and Hoffmann deny this.

Storch saw an interruption of pertussis with an outbreak of smallpox.   Vogel reported the opposite, that children with whooping-cough were immune to smallpox.   According to others, smallpox patients were attacked by pertussis only after the pustules had dried up. Richter mentions one case where a child was cured of a long-continued whooping-cough by smallpox.   Blache saw the course of pertussis become more severe on the appearance of a smallpox epidemic.   Danz denies that either disease has any influence on the other.

DIAGNOSIS.

AFTER the convulsive stage has made its appearance, it is impossible to confuse whooping-cough with any other disease. Moreover, during an epidemic the prodromal stage may even be diagnosticated, or at least suspected, by certain symptoms which we have already described. At the same time, it usually requires a paroxysm to induce absolute certainty as to the nature of the disease. In its outspoken form the coughing paroxysm is so characteristic that the physician may make his diagnosis of whooping-cough without fear of error, if only he does not forget at the same time to acquaint himself with the course of the disease, and to consider the periodic recurrence of the paroxysms, the free interval with almost perfect well-being between them, and the occurrence of other cases of whooping-cough in the vicinity of his patient.

In cases where the physician himself has no opportunity to observe a paroxysm, or in case this is not characteristic, the diagnosis may be in doubt. Atypical paroxysms occur especially in nurslings, in whom, as A. Roe has mentioned, the stridor is often wanting. A good description, or imitation, of the paroxysms by a third person in case of necessity is often sufficient.

Hysteric simulations and reminiscences of pertussis are, apart from an epidemic, easily differentiated; in the course of one, sometimes with great difficulty. In doubtful cases hysteric pertussis may be recognized by the imperfect very exaggerated imitation, by the omission of a catarrhal stage, and of vomiting after the attack, and by the striking effect of suggestive measures on the number of paroxysms or their duration.

As an example of the last, Bandisch's case may be mentioned, in which a young woman suffered for two years from whooping-cough, and the physician had been so successful with his treatment that an attack occurred only every five or six days. According to Priou, Biermer describes an extreme case in which the patient suffered four years. But here the disease had progressed to such a degree that the patient, a woman, had sixteen attacks every twenty-four hours, during which she emitted 62,000 to 64,000 forcible expirations.

In general, hysteric paroxysms last much longer than true ones, sometimes for even an hour with but slight intermissions. During the night the attacks usually cease, but not always so, as Biermer pointed

out. The amount of expectoration is small, and vomiting and hemorrhages are but occasional accompaniments.

The expiratory explosions follow one another less rapidly than in whooping-cough, and the intervening inspirations are full, though not long drawn out. Closure of the glottis, with the resulting stridor, may be wanting, but, contrary to Biermer's assertion, it is in many cases present. In favor of true whooping-cough, in contradistinction to the hysteric form, a preceding catarrhal stage and childish age tell, but only to some extent; but the most important elements in a differential diagnosis are the absence of hysteric stigmata, and the presence of the stigmata of whooping-cough, which we are about to describe. These are the ulcer on the frenum linguæ, the dark blue discoloration of the upper eyelids that often remains till the termination of the fastigium, petechiæ and ecchymoses on the face and neck, especially hematoma of the upper eyelids, and ecchymoses of the conjunctivæ, continual edema of the face, and, finally, a point on the larynx on pressure of which the attack may be frequently called forth.

Omitting the laceration of the frenum and the laryngeal exciting point, these stigmata may be the result of a suffocative epileptic or hysteric attack, or of an attempt at strangulation, and therefore their value in the differential diagnosis of pertussis from other paroxysms of coughing is little or nothing. In a doubtful case of confusion between epileptic and whooping-cough paroxysms, it is to be remembered that in the latter petechiæ and ecchymoses are limited almost without exception to the head and neck, while in the former they are seen on the chest, shoulders, and sometimes on the contorted limbs.

Although we consider it almost impossible, omitting hysteric pertussis, that a careful opinion should err in the diagnosis of whooping-cough, yet we intend to contrast a few diseases that seemed to confuse the older writers, and which might perplex the inexperienced, in order to bring out the typical picture of tussis convulsiva epidemica.

Feiler first, and so far alone, described and differentiated an epidemic cough under the name *tussis ferina*, or dry cough ("Schafhusten"), which attacked nurslings, also older children, and appeared in violent paroxysms associated with intense effort and imminent danger of suffocation, but without the peculiar inspiratory stridor of whooping-cough. The attacks terminated with expectoration of mucus, but without vomiting. The course of the disease was very mild. It is evident that only an epidemic of such cases apart from a whooping-cough epidemic could dismiss the suspicion that they were mild cases of pertussis.

Tussis spasmodica, convulsive cough, which was at one time considered a special disease, is nothing else than a symptom of laryngeal inflammation. The name might perhaps be useful in designating those cases in which the convulsive coughing fit does not associate itself accidentally

with an existing sporadic laryngitis, but occurs epidemically and idiopathically. These epidemics do not confine themselves to the age limit of tussis convulsiva, but attack with almost the same frequency adults and the new-born. The paroxysms are ushered in by a tormenting irritation of the throat, they occur irregularly, but especially after meals and on lying down at night. Stridor is absent. Sometimes they are so frequent that they lead to profuse sweating and heart-weakness, and then are dangerous. Catarrhal inflammation of the upper respiratory tract may precede, accompany, or follow the cough.

We find this description from a number of epidemics in the fifteenth, sixteenth, and seventeenth centuries, under the name " coqueluche," " catarrhus epidemicus," " tussis ferina," etc. We personally saw the disease at the end of the winter 1894–95 toward the termination of a grippe epidemic, in many persons who had escaped the influenza. In one pregnant woman the violent cough was unquestionably the cause of a miscarriage at the eighth month. Codein, and especially potassium iodid, were found effective in many cases; mild cauterization of the laryngeal fold was useful in others.

Croup, or the "suffocatio stridula" (Home), " cynanche trachealis" (Rush), " angina polyposa membranacea" (Michaelis), " Hühnerweh" (chin-cough), " häutige Bräune" (membranous sore throat), as an independent laryngeal inflammation, or as a symptom of angina diphtheritica, has been often confused with whooping-cough by Kurt Sprengel, Danz, and many others. The many so-called pertussis epidemics, in which a countless number of children perished by suffocation early in the disease, were in great part croup epidemics, and only exceptionally whooping-cough complicated by a malignant and extremely acute laryngitis. Since Wichmann's immortal treatise on " Millar's Asthma and Membranous Sore Throat" a confounding of croup with whooping-cough ought not to be possible. The acute feverish condition of the child, the continuously difficult, long-drawn-out, anxious respirations, with the fine, high, crowing inspiration, which becomes evident especially on deep breathing, or an attempt to talk, and during the paroxysms of the guttural or rattling cough when endeavoring to expel mucus or the false membrane; the hoarse, muffled, and sometimes inaudible voice; the excruciating anxiety—enduring for hours at a time—of the suffocating, deadly pale, or livid child is a picture that cannot be mistaken for whooping-cough.

Pseudo-croup, " angina laryngea," "laryngite striduleuse" (Guersent), " angine striduleuse" (Bretonneau), "laryngite spasmodique" (Rilliet and Barthez), is simply a symptom of beginning laryngo-tracheitis. This takes healthy children suddenly at night with a hoarse croup-like cough, accompanied by whistling inspiration. The attack is repeated during the same or in the following night, and then becomes a simple catarrhal condition. During the intermission, the respirations are a little hastened and there is slight feverish excitement. The condition, according to Rosén von Rosenstein, and as is well known, frequently precedes the commencement of measles or the eruption of its exanthem. More rarely it appears as the forerunner of an outbreak of urticaria, in place of the simple edema of the glottis, which is more common in this country (Germany).

Spasm of the glottis (" Glottiskrampf"), " spasmus glottidis," " laryngismus stridulus," occurs especially in children of nervous parentage who have been lately weaned, under the influence of dentition, and, above all, in the course of rickets. It begins without prodromes, and manifests itself

as a convulsive closure of the glottis with symptoms of imminent asphyxia, cyanosis, eclamptic twitchings, and convulsions of the limbs. It terminates at the height of the danger after half a minute or one minute, or even longer, with one or more long-drawn-out crowing inspirations. This is repeated at irregular intervals, on any physical or mental excitement. The attacks are often numberless.

It forms a not uncommon complication of whooping-cough and must carefully be differentiated from it on account of the disturbing influence which it has on the prognosis of the course of whooping-cough.

Asthma periodicum (Millar), "asthma spasmodicum" (Rush), "Millar'sches asthma" (Wichmann), attacks almost exclusively perfectly healthy children between two and seven under the symptomatology of an ordinary catarrh with hoarseness and slight fever. During the first two days a violent dyspnea comes on suddenly, usually without cough. The extremely difficult respiration is accompanied by a deep, low sound. The paroxysm is most agonizing, lasts some hours, and disappears gradually, only to return with increased vehemence after an interval of twelve, eighteen, or at most twenty-four hours with a higher fever and a small feeble pulse. After repeated attacks, during which the efforts of all the respiratory muscles, the harrowing apprehension, and the convulsive twitchings of the limbs become more violent, within the first eight days death or recovery ensues.

This can scarcely be confused with whooping-cough. It is differentiated from pseudocroup by its cyclic course and its independence of the appearance of that affection.

Acute edema of the glottis, as it occurs in children from accidental aspirations of hot steam (from the water-kettle or tea-pot), from swallowing hot fluids, or from inflammatory, particularly ulcerous, affections of the throat, tongue, larynx, during the course of a nephritis, at the beginning or height of urticaria, from the use of iodin, has been seen now and again as a complication of whooping-cough, and adds a greater danger than the disease itself. The protracted dyspnea with aphonia, the low whistle on every inspiration, the open-eyed, quiet, anxiety of the pallid, deathly cold child, present a picture not to be confounded with pertussis.

A *convulsive cough*, induced in many cases by bronchial *adenopathy*, caused Guéneau de Mussy to look for the origin of whooping-cough in an inflammatory swelling of the bronchial glands. A similar cough is now and then a symptom of aortic aneurysm also. In sporadic cases of pertussis this may be of value in the case of both children and adults.

Ictus laryngeus, "vertigo laryngea," is likewise not to be forgotten. This, according to Gasquet, Charcot, and Gerhardt, occurs especially in asthmatics, habitual smokers, the gouty, and those subject to laryngitis. After a sort of burning sensation in the larynx, the attack begins with cough, sometimes violent enough to produce cyanosis, sometimes of milder character, and then the patient suddenly falls to the ground, generally with relaxed limbs, less frequently with epileptic twitchings, which may cause the paroxysm to simulate Jacksonian epilepsy. The attack is usually short, and the patient at once recovers. It may be repeated twice to fifteen times daily. This condition may be confounded with whooping-cough only by the most superficial observer looking at only single symptoms of the disease. At least we might judge so, if so celebrated a physician and investigator of whooping-cough as Heberden had not left behind the following sentence on pertussis in adults: "Adulti, accessione victi, mo-

mento temporis velut attoniti concidunt; illico vero resipiscunt, atque hoc est proprium huius affectus signum in adultis." Is this the first observation on ictus laryngeus?

According to many writers, foreign bodies in the respiratory passages may produce violent paroxysms of shrill coughing with hemorrhage and vomiting, which therefore have a certain similarity to whooping-cough. In regard to this, Biermer records an especially remarkable case. A man sleeping with open mouth breathed in a bed-feather which occasioned a bronchitis lasting for six months, with violent paroxysms, until the discharge of the foreign body in a convulsive attack resulted in recovery within a few days.

The paroxysmal appearance of a jerky cough is seen not rarely in *chronic follicular pharyngitis* and *elongation of the uvula*. But the absence of the inspiratory stridor, the local inspection, and the course should prevent an error in diagnosis.

All the above-mentioned cough affections are liable to be confounded with whooping-cough only by those who are looking for one symptom and forget the general picture. This error is responsible for the numerous false diagnoses of historic epidemics of coqueluche, influenza, croup, etc., for pertussis. This confusion has also led to many false opinions in regard to true whooping-cough.

This clears up, for instance, the observation of Danz, repeated by almost all subsequent writers, that the cause of tussis convulsiva was responsible for general feebleness, rickets, and dropsy, because Danz considered the inspiratory crow of spasm of the glottis, of rachitis, of edema of the glottis in nephritis, etc., to indicate true whooping-cough. It appears that it was he, too, who first recognized and put a stop to the fine distinctions in vogue between whooping-cough, or blue cough, and Eselshusten, dry cough, chin-cough, etc.

EPIDEMIOLOGY.

THE occurrence of a case with the previously described symptoms is not sufficient to make the diagnosis absolute. The following conditions must also be fulfilled.

Whooping-cough is an epidemic disease. It attacks simultaneously several individuals living in close proximity and from this focus spreads far and near. Sporadic whooping-cough is decidedly doubtful. When an individual is attacked by a cough, even though it agrees in all its symptoms with pertussis, if it is not prevalent, and does not become epidemic, the diagnosis is suspicious. An epidemic may be limited to the smallest circle or attain extraordinary dimensions. It may attack a house, a street, a village, a city, or extend over large tracts of country, and occasionally, with wonderful rapidity, become pandemic.

Whooping-cough attacks individuals usually only once. To have had it is a protection for every future epidemic. Stoll, Danz, Sprengel, and other writers have endeavored to disprove this on "internal" grounds, but unsuccessfully. At least a repetition of the disease in the same person is extremely rare; much rarer, for instance, than a repetition of measles. Rosenstein in thirty-eight years' practice saw no case, and Cullen, Hufeland, and Matthaei inquired among old people in vain for an example of recurrence. That the strictest rule may have exceptions, is acknowledged: "Curavi nonnullos," says Heberden, "qui mihi fidem fecerunt, se bis eo (tussi) fuisse implicitos." Jahn asserts the same thing, and Schönlein saw in several epidemics adults with a second, though an abortive, attack. Lühe observed in his own family, which was apparently very susceptible to the disease, a second attack in one of his children two and one-half years after the first attack, and a second in the child's mother. We have already discussed the question of relapsing whooping-cough.

Whooping-cough attacks almost exclusively children. This is probably because the frequent recurrence of the disease in the course of years finds only the young children who have not been attacked susceptible. Moreover, this is supported by the fact that in newly discovered countries, uninfected till the arrival of Europeans, whooping-cough, like other infectious diseases, respects no age, and works havoc among adults as well as children. It is likewise probably true that

the age of greatest morbidity is the fourth year, while the epidemic ordinarily recurs every two or three years. Nevertheless, in cities and countries where whooping-cough prevails epidemically every year—for example (according to Ranke), in Munich—the age of predilection is also the fourth or fifth year. And if there is added to this the fact that children are seldom attacked under the second year, it must be assumed that a certain predisposition depends on age.

According to the most careful observers (West, Blache, Lacroisade), the most susceptible age is from two to five. Between six and ten the disease becomes rare, and after the first decade it is seen only exceptionally. Isolated cases have been reported in nurslings. Biermer collected several cases from the literature of the subject. Bouchut mentions a case in a new-born child who was attacked on the second day, began to cough on the fourth, and manifested outspoken symptoms on the eighth. Watson reports another where it was evident on the first day of life. In this case the mother had in the last weeks of pregnancy been taking care of a child with whooping-cough. Rilliet and Barthez record violent paroxysms on the first day in a child whose mother during the last month of pregnancy had suffered from whooping-cough. In Scotland, Gibb affirms it is the general opinion that the disease may run its course during the fetal period, and that a child whose mother had whooping-cough during pregnancy remains immune throughout life.

Heberden, Gibb, Velten, and others have reported whooping-cough in old age; the first-named in a woman of seventy and in a man of eighty, the last-named in a man of seventy (Dissertation of Bruno Claus).

Apart from a certain age and an acquired immunity, there is no absolute protection against whooping-cough. It is true that, according to all statistics, females are more susceptible than males, to such a degree that about twice as many girls are attacked as boys (Blache, Rilliet and Barthez, Hagenbach, Baginsky), which is all the more remarkable when it is remembered that more boys are born than girls. Moreover, among adults women, and among these especially the pregnant and wet-nurses, manifest an increased susceptibility (Biermer); yet in this there is no protection for males. Unquestionably feeble, especially rachitic and scrofulous children, are more commonly attacked than healthy ones (Ettmüller, Jahn, Biermer). The observation is likewise general that such children are not only more frequently attacked, but are attacked more severely, though Lochner, it is true, reports the opposite from a summer epidemic of 1865. We personally can vouch

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for the fact that apparently healthy children with tubercular family history suffer more intensely, die more frequently, or succumb more commonly to complications or sequelæ. Nervous and excitable children manifest more violent paroxysms than those of rougher constitutions. The report of Wimmer and Meissner is worthy of mention, namely, that deaf-mutes and blind children show milder attacks than those possessed of all their senses. They assert that with the absence of a sense organ there is a defect in the development of the respiratory organs, making them less liable to injurious influences. A certain amount of protection is undoubtedly afforded by the institutions in which they usually are.

Lühe's communication makes it probable that a particular family susceptibility may exist.

A violent epidemic recognizes no difference in sex, constitution, or hereditary qualities. The more acute its development, the fewer escape among all who come in its way, and prophylactic dietetic treatment avails nothing. The credulous Jahn reports that in severe epidemics, even the dogs and cats were affected.

The spread of whooping-cough is limited to no definite time, no season, no weather conditions, yet the severity of the disease may change with these circumstances. According to the statistics collected by Hirsch, epidemics are most frequent toward the end of winter and the opening of spring, less frequent in autumn and winter, and rarest in summer, yet no season completely excludes their appearance. If the epidemic begins in autumn, it may continue into the winter, or even into the spring or summer. In regard to this, the aphorism of Hippocrates, "æstivos morbos superveniens hyems dissolvit et hyemales æstas succedens transmutat," is applicable in so far that with the change of season the number of attacked decrease and individual patients experience an improvement in their condition. According to Hirsch, the greatest frequency of the disease over the whole world is seen in summer and autumn.

A beginning epidemic is favored by nothing so much as a change of weather by which a sudden continued cold period, never reaching the freezing-point, is made to follow moist warm weather. Schönlein reported the increase of endemic whooping-cough, and the breaking-out of the epidemic form especially, in the months of March and April, when green Christmases were followed by white Easters, and in the late autumn, when weeks of rain were suddenly succeeded by the fore-winter with a constant fluctuation of temperature between 2° or 3°

and 15° R. (35° or 40° and 65° F.). Moreover, a southwest wind veering to northwest and cloudiness seem favorable to the virus.

In the tropics and subtropic regions whooping-cough is much rarer and less severe than in northern climes. A raw climate causes the course to be especially dangerous on account of inflammatory complications in the chest organs.

The geologic formation of a country has no influence on epidemics as far as is known (Hirsch).

The spread of whooping-cough occurs by contagion. An autochthonous development cannot be denied, yet its conditions are unknown. There is more discussion even to-day than formerly as to whether the disease develops outside the human body as a miasm; and if it does, what are the circumstances necessary for this development. The fact that regions lying on the sea, drained by rivers, and covered with clouds (England, Sweden, northern France, especially Paris, the banks of the Rhine, of the Elbe, of fresh-water basins like those on the northern slope of the Alps), suffer most intensely from whooping-cough, leads inquiring physicians like Schönlein to conjecture that they must be regarded as the home of the virus. Some compare the virus of pertussis with that of malaria, but others, entirely disregarding the theory of a miasm, contend that every case of whooping-cough happens by transference from one sick of the disease to the healthy. Yet if we recall that such painstaking and conscientious observers as Stoll, Mellins, Meltzer, Sprengel, and Laennec deny the contagious transference of pertussis, it can scarcely be doubted that the disease is not always and in every epidemic contagious. That it is very frequently, even commonly, conveyed by contagion, as Holdefreund, Hufeland, Paldamus, Schönlein, and Autenrieth assert, is sufficiently evidenced by the present-day endemics and epidemics.

Some bring forward the fact that mothers (Haasse), wet-nurses, and maids who take care of children are attacked, as a proof of its contagiousness. Butter and Rosenstein saw examples of transference across the sea. Moreover, the repeated epidemics appearing in Iceland and in the Faroe Islands can on every occasion be referred to the introduction of the disease by fishermen who once a year visit these islands from northern France and other countries. Chalmers introduces his description of the whooping-cough epidemic in South Carolina in 1759 with the explanation that the disease is not endemic to this region, but has raged three times within twenty-six years after being introduced.

The fact that it is possible to avoid the disease by avoiding contact and intercourse with patients speaks also for its contagiousness.

In relation to this, Dugès, Häussler, Blache, Lombard, and Bouchut have reported very convincing cases. F. Beyer quotes the case previously mentioned by Bouchut: A woman who had just been delivered (August, 1843) received a visit from a relative. This visitor brought with her a child in the ninth week of whooping-cough, who remained in the house of the new-born but one day. On the second day the baby began to cough, and eight days later manifested typical paroxysms. No other case of whooping-cough had entered the house.

In Häussler's case a small child took the disease from a tramp, and up to this time there was no trace of pertussis in the city. The immediate neighbors were infected by the child, and eventually the disease assumed epidemic proportions.

The spread of whooping-cough from place to place often proceeds so slowly that it can be traced with certainty. Thus, Friedrich Jahn describes an epidemic in 1805 in Saxe-Meiningen introduced into the city by a hunchbacked woman: "After the numerous members of this woman's family had been infected, the disease spread throughout the same street, and thence over the city with such intensity that the youngest children and oldest people did not escape; a number were attacked severely, and not a few died."

Josef Franck observed in regard to whooping-cough, in 1823, as well-known facts: "Propagatur (sæpe per ipsos medicos) morbus de ægro ad ægrum, de domo ad domum, de pago ad pagum, ita ut via, quam sequitur, erui et demonstrari possit, eoque quodam in loco stabilito—in orphanotropheo, instituto, familia, urbe, provincia—vix antea, quin omnes infantes ad illum dispositi ægrotaverint, cessat."

Whether contagion takes place through a fixed medium, or one capable of circulating in the atmosphere, is uncertain. Many theories have been advanced, but proofs are lacking. Almost all agree that the coughed up mucus contains the contagious material.

The possibility of limiting the disease to individual houses, apartments, flats, streets, etc., seems to show that the virus is not capable of circulating to any great extent in the atmosphere. The cases of immediate contagion, of which many are known, confirm the same hypothesis.

According to Walshe, Biermer relates the following case: A lady left a port on the eastern coast of England with her two children, who were at the time suffering from whooping-cough. The ship stopped at St. Helena, where the soiled linen of the children was sent ashore to be washed. The children of the washerwoman were infected with pertussis, and from them it spread over the whole island, where for a long time previously no case of the disease had been met with.

The indirect transmission of whooping-cough by physicians seems to be anything but rare, according to Josef Franck, and the following

from Rosén von Rosenstein: "I know an instance where whooping-cough was carried by a messenger from one who had the disease to two children in another house. Moreover, I recollect another case where I myself unintentionally carried it from one house to another."

Direct transmission by a dog suffering from whooping-cough has been mentioned by Jahn. That dogs are susceptible to the disease has been reported by many early writers. Peter Lehnen adduces an observation from the Würtemberg "Medical Report" of the year 1872 to the effect that a three-year-old dog was infected by a child, and, after suffering for four weeks, it succumbed to the prostration resulting from the frequent vomiting. Th. Smelz reported in 1867 a case in a dog where the course of the disease was so carefully observed and described that there can be no doubt as to the correctness of the diagnosis. Melhose narrates from an epidemic of 1836 the fact that dogs living in the sick-room were in almost every instance infected. In an epidemic in 1804 Jahn had seen cats as well as dogs suffering from the disease.

These observations, apart from their epidemiologic importance, are especially significant because they corroborate the assertions of several investigators that they conferred pertussis on dogs and cats by inoculation of the sputum of animals suffering from the disease. We will take up in another section the inoculation experiments of Letzerich, Afanassieff, Schmelz, Deichler, and others, and only mention here that they too confirm the assumption that the contagium is associated with the expectoration. Tschamers too was successful in inoculating himself and a working-man. Though in contradiction of these, stand the negative results of the experiments of Birch-Hirschfeld and Rossbach.

That the disease is highly contagious at the height of its course seems certain, but that the patient is dangerous as long as he coughs, as some writers affirm, is doubtful, though for the sake of prudence it is better to assume this. According to Rosenstein, Schönlein, and others, in different epidemics the contagiousness is very different.

The mode of entrance of the virus has not been absolutely determined. That it is through the respiratory tract is nothing more than a conjecture, which would become probable only if the contagium was shown to be a volatile substance.

ETIOLOGY AND PATHOGENESIS.

THE specific nature of whooping-cough cannot be doubted after an unprejudiced study of the epidemics. The transition of other diseases into pertussis has been asserted, but not proved.

Styx was probably the first to affirm that whooping-cough was nothing more than an ordinary catarrh, and that any catarrh might develop into pertussis. Since then, many have asserted this without realizing how contrary to the facts their opinion was. A catarrh may progress from the upper respiratory tract downward, even to the lung itself, but that it may be transformed into whooping-cough is not true. And it can scarcely be understood how a clinician like Wunderlich could fall into this error. "Whooping-cough may develop, as a secondary affection, from other diseases in which a catarrh exists, as measles, tuberculosis, or an ordinary bronchitis of indifferent origin, by the catarrhal cough becoming more and more convulsive-like, and finally appearing as outspoken pertussis. This is often difficult to prove with certainty, yet in isolated cases it cannot be doubted."

Even if the transition of an ordinary catarrhal cough into a pertussis-like cough was observed, it would not be advisable to make the similarity of two symptoms equivalent to an identity by putting them under the same name, before this identity was proved to be true in all symptoms of the disease. Until such a time, the designation pertussis-like paroxysm ("Toux coqueluchoide," Grancher) would be sufficient.

Pohl's opinion that, because whooping-cough begins with injected eyes, sneezing, and coughing, it is nothing else than altered measles in which the virus attacks especially the stomach and diaphragm, would not be worth mentioning if it had not been carried further by others. After Volz and Josef Franck, particularly, had expressed the same view, and the latter had reported an acute eruption on the bronchi in pertussis, his most celebrated pupil, Autenrieth, in all seriousness, affirmed that the virus of whooping-cough was only the diluted contagium of measles, as the virus of measles was the condensed contagium of whooping-cough. He even succeeded in separating the material contagion of the disease from the body of the patient, obtaining the virus from the lymph of pustules which he generated by rubbing his tartar emetic salve into the epigastric region, and so transferred the disease by inoculation to healthy persons. Others following him were not successful. This hypothesis as to the relationship of whooping-cough and measles was overthrown by Berndt and Schönlein by the mere statement of the fact that one disease did not protect from the other; on the contrary, favored the development of it. In the mean time this theory was being promulgated through France. Aberlé in 1816 saw a whooping-cough epidemic in association with measles, and this coincidence being repeated several times in the following years determined his opinion that pertussis was an altered measles. Rilliet concluded the same from the Geneva epidemics of 1847, 1850, and 1851. When about that time (1854) Germain

Seé defended this hypothesis with the greatest confidence on statistical and "internal" evidence, clinicians like Archambault failed to see its preposterousness, and fell into line. In addition to Schönlein's argument, the simple fact brought forward by Hirsch, that in 495 whooping-cough epidemics the coincidence of measles was only 94 times observed, contradicts any close relationship between the two diseases.

On account of the periodic aggravation of the disease on every third day, which Girtanner thought he observed, this author formulated a hypothesis that the miasm of whooping-cough stood in close relation to that of malaria. He even went further, and asserted that the miasm of both was identical. Rosenstein also, and many others after him, mention the "typus tertianus" of pertussis; though Stoll, Matthaei, and others failed to find it, even after their attention had been called to it. Moreover, we no longer see it in our day. And though on this account its occurrence in the past cannot be denied, it was in any case of not sufficient importance to the disease to conclude from it a relationship with malaria. "Contingit nonnunquam ut febris intermittens huic tussi jungatur, sed dispares semper hi morbi erunt" (Stoll).

In the comparison of the exciting cause of whooping-cough with the miasm of malaria lay at least the germ of the thought which prevails to-day for all epidemic diseases—namely, the thought of an external noxious agent forcing its way into the body. This was first proposed by Rivinus and Linné. A pretty clear notion of the effect of this noxious material or agent was given by Rosén von Rosenstein in his addition to Linné's work on the origin of whooping-cough through living insects:

"The true cause of this disease is a foreign substance or seed that has the power of increasing like the virus of smallpox, and attacks children who have not been previously infected with it. I am indeed uncertain whether it may be an insect. Still, it is evident that the virus is transplanted by contagion, and that a part of it obtains entrance to the chest by inhalation, though most of it settles in the stomach, being swallowed with the saliva. In both places, but especially the latter, it attacks the nerves and irritates them at certain hours, though again it may remain at rest for half a day. This irritation causes, through the medium of the nerves, a convulsive cough that continues till the most effective part of this excitant has been thrown off in the vomit. And it entirely ceases only when this excitant is killed and rendered powerless, or discharged from the body. It follows, therefore, that to cure whooping-cough such means must be employed as will kill and render innocuous the excitant, or get it out of the body by the shortest way."

Since Linné and Rosén von Rosenstein, the theory of a miasm and living contagium has been repeated anew, and again refuted.

Linné's "insects" have taken on only a different form according to the investigator. Some follow the view of Heberden and Paldamus, that the contagium of whooping-cough behaves "like the venereal virus of syphilis"; others share Canstatt's opinion that the disease is spread by

means of an atmospheric miasm like influenza, to be sought for some-times in the expired air, again in the fluid excretions of patients. Thus Poulet, in 1867, believed that he found the agents of the disease in a Monas termo and a Bacterium bacillus cultivated from the expired air of those afflicted with whooping-cough. In the following year Binz and his pupil Jansen found, on examination of the sputum, small forms with long whip-like processes, though they left it undetermined whether these were misshapen mucous corpuscles. Letzerich then came forward confidently, with small reddish-brown bacteria from the sputum which he cultivated on a bread and milk pap, and which, when inoculated, into the tracheæ of young dogs and cats, produced the disease. These animals, after six or eight days, manifested "genuine convulsive paroxysms of coughing." While Henke was confirming Letzerich's statements, Birch-Hirschfeld found the bacteria of this observer also in the pus, in the urine of vesical catarrh, and in the sputum of simple bronchial catarrh. He succeeded also in producing attacks by inoculation, but these attacks were in no way typical. Tschamer described small organisms, the size of the point of a needle, which he found making a network of spores on the vocal cords and down the trachea. He cultivated them on potatoes and bread, and made a successful inoculation on himself. Since Tschamer's bacteria have been proved to be identical with the Cap-nodium citri, which forms a blackish-green deposit on decaying apples, oranges, and lemons, the origin of his whooping-cough bacteria is evident. Yet soon afterward Burger discovered a bacillus, Afanassieff other bacilli, Deichler again amœbæ, Ritter diplococci, Cohn and Neumann "Stäbchen" (bacilli) as a cause for whooping-cough; and they all, remarkable to say, succeeded in producing pertussis by their different organisms, though Rossbach inoculated the sputum itself in vain.

Though the miasm and contagium of whooping-cough remain yet to be discovered, the expectation is well founded that the solution of the problem will fall to the lot of bacteriology; for its epidemic origin, contagiousness, cyclic course, immunity after one attack, and, finally, the favorable effect of quinin on the disease (as shown by Binz), all point to the analogy of pertussis, as to its causation, with other infec-tious diseases.

Granting that this theory corresponds to proved facts, the question arises whether whooping-cough is to be regarded as an originally local disease or as a primarily general one, in the course of which the mani-festations become confined to one spot. So far, we possess no absolute facts that answer these questions. The absence of enlargement of the spleen argues for the first hypothesis, but the catarrh in the first stage, and the enlargement of the lymph glands at the root of the lung, as frequently demonstrated postmortem, witness for the second.

The experiences of late years in regard to secondary general extension of gonorrhea, which almost always remains localized, have changed our views in relation to the secondary invasion of other organs by a primarily local infection. And the pathogenesis of whooping-cough is facilitated

if a comparison is instituted between the virulent urethral inflammation and the chorea gonorrhœica on the one hand, and the prodromal bronchial inflammation and the subsequent convulsive stage on the other. Or it may be considered that the nervous stage is dependent on the catarrhal stage in a manner analogous to the dependence of the nervous paralyses after diphtheria on the intoxication produced by the primarily localized focus of Löffler's bacillus.

Yet both these hypotheses signify little more than many others formulated in the course of time in relation to the nature of whooping-cough, except to add two more to the list. The hazarded conjectures are almost numberless. Gibb has collected them up to the year 1854, and he mentions over one hundred.

Three dogmatic assertions cover the hypotheses of all writers: namely, whooping-cough is an infectious disease; it is a neurosis; it is a laryngotracheal catarrh. The majority of physicians still believe that it is necessary to decide in favor of and to defend one or other of these, and but few endeavor to combine them. Yet nothing seems more natural than to say: Whooping-cough is an infectious disease as regards its external cause; it is a catarrh as regards the anatomic localization of its most marked disturbances; it is a neurosis in relation to its most prominent symptoms.

The discussion is practically nothing else than a change of opinion by different physicians and at different times as to whether the etiologic, anatomic, or nosographic consideration of the disease is to be regarded as the most important. We cannot attempt to decide this point here.

With a few, especially the older writers, the real question lay deeper. The point as to whether whooping-cough was an infection, neurosis, or catarrh of the respiratory tract, was applied directly to the essential cause of the disease. That is, they endeavored to ascertain whether whooping-cough was an exogenous or an endogenous disease. In other words, was the agent coming from outside, or was the internal secondary groundwork produced by it of more importance in the causation of the disease? And in the former case, is this external cause a specific or a general source of mischief?

Compare whooping-cough with tetanus, and it must be regarded as an infectious disease attacking particular parts of the nervous system. Put it alongside an ordinary catarrh due to "cold," and there remains to be explained why the typical coughing paroxysms take place in one and not in the other. But look at it as an epidemic of hysteric convulsive attacks produced in nervous subjects through a psychic contagion, and the catarrhal stage becomes only an accidental forerunner of the disease which seems to make the particularly predisposed individual susceptible to the mimicry of coughing, and to extravagant explosions of the same.

To decide in relation to these three possibilities, all of which have a distinguished following, is not a matter of indifference, since a rational treatment depends upon it. Without going further, it is easy

to see that an infection would require specific treatment; a local irritation of the mucous membrane, local treatment; a psychico-nervous cough, psychic treatment, in order to meet the "indicatio causalis."

We have, however, already felt ourselves obliged to decide that whooping-cough is an exogenous disease produced by a specific exciting cause, and the facts leading to this oppose so strongly the earlier opinion, that whooping-cough is an endogenous disease, that we find it unnecessary to take this into consideration at all.

In the further investigation of the case we have only to answer the question, How are the different symptoms in the course of whooping-cough to be explained? Or, in other words, Where is the anatomic seat of the disease to be sought?

During the catarrhal stage, whooping-cough is without doubt primarily a catarrh of the upper respiratory tract; during the convulsive stage it is as unquestionably an irritative condition of the nerves presiding over the respiratory function. While some writers assert that the catarrh of the first stage continues throughout the second, at least as regards its local effects, and that these local changes are sufficient to explain the whole second stage, others deny that the convulsive stage could be produced by inflammatory or other local change, and affirm that a particular irritability of definite nerve tracts, and an excitation of these, are necessary to its production.

The first opinion was defended by Whatt (1813), Badham (1814), and Marcus (1816). These writers went so far in the defense of the catarrhal nature of the whole disease that they denied any peculiarity to the cough in the convulsive stage of whooping-cough in order to classify it with ordinary bronchitis. But it was really after Broussais with his great influence (1814) had interpreted whooping-cough as a bronchitis with a marked irritability of the inflamed membrane that this opinion gained ground, and it spread even the more readily because, according to Wunderlich, the localizing doctrine of diseases, introduced by Broussais, was to be applied also to whooping-cough and led to new anatomic investigations about the latter. Yet while Desruelles (1827), Dugès, and others were defending the inflammatory nature of whooping-cough, even though in a somewhat different way, and strove to prove it anatomically, the writers who succeeded them were proposing and stating grounds for the view that *the anatomic changes found in the respiratory tract of the cadaver were not due to pertussis, but only to its complications.*

Though, in the consideration of this fact, they seem to overlook or to misinterpret somewhat the catarrhal stage of the disease, they succeeded in demonstrating, at least from the point of view of treatment, what was of the greatest importance, that the principal danger in whooping-cough lay in the occurrence of complications, especially severe bronchitis and pneumonia, the more accurate diagnosis of which had been

made possible by Laennec. They therefore directed the attention of physicians particularly to these, while allowing nature to take care of the neurosis.

The theory which regarded the pertussis paroxysm as a symptom of a nervous disease was first put on a firm basis by Hufeland in 1793. He pointed out the foreboding aura to a paroxysm, the frequent occurrence of convulsions and other nervous attacks, the radiation of the irritation to the nerves of the stomach, and the whole form and general appearance of the attack. It was he, therefore, who first called attention to those very phenomena which were brought forward by Romberg fifty years later with greater good fortune.

In the mean time, the knowledge of nerve conduction was extended *so that the assertion that something was caused by a functional nervous disturbance was no longer sufficient, but it was necessary to determine the locality in which the disturbing influence originated, and the route that such a morbific impulse would take in order to produce irritative symptoms.* We know that each motor impulse is the result of conduction along special nerve tracts, and that each involuntary motor explosion has its cause in the irritation of a centripetal nerve.

Now, as regards the different forms of cough, no one doubts that the centripetal cough nerve is ordinarily the vagus, and the centrifugal tract is always the innervation system of the epiglottis and the diaphragm.

That the filaments of the vagus in the mucous membrane of the larynx, trachea, and bronchi are the receiving system by which cough may be excited normally on irritation, has been proved experimentally by Krimer, Cruveilhier, Romberg, Budge, Rosenthal, and especially by Nothnagel. The last-named demonstrated that the mucous membrane of the regio interarytænoidea and the bifurcation of the trachea were the parts most susceptible in the production of cough on irritation, while R. Meyer designates the regio arytænoidea as the only place. (He calls it the "Hustenstelle.")

Yet not only did the old writers rightly conclude, but recent experimenters have placed beyond doubt, that every peripheral filament of the vagus, especially when its irritability is increased by disease, may transfer irritation to the expiratory tracts in the form of cough. For proof of this it is only necessary to call attention to the excitation of cough by irritation of the costal pleura (Kohts), the external auditory passage, the root of the tongue, the pharynx, the esophagus, the stomach (Bull), the liver and spleen (Naunyn), the nerves of the skin (Brücke, Ebstein), the sensory branches of the trigeminus of the nose (Sommerbrodt, Schadewald, Wille), the uterus (Hegar), and the mammæ and ovaries (Strübing).

The chief question in relation to the attack in whooping-cough is, Does the paroxysm arise at some spot along the peripheral distribution

of the vagus, or other sensory nerve? and, if so, where is this located? Or is it a centripetal tract higher up that is irritated and conveys the impulse to a centrifugal tract? In the latter case it must, first of all, be determined whether this area of disease excitability is represented by the peripheral neuron from the sensory endings to Gallois' center, the "nœud vital" of Flourens (that is, to the cough center of Kohts under the ala cinerea), or by the central neuron from the medulla oblongata to Christiani's expiratory center in the substance of the anterior corpora quadrigemina, or whether the impulse reaches the centrifugal tract from the cortical (Munk, Semon, Horsley, and others) or transcortical region.

These questions, even though formulated less exactly, have occupied the attention of investigators into the seat of the cough paroxysm since the time of Willis.

Since Willis placed the seat of irritation in the chest; Harvey, Huxham, Basseville, Unzer, Stoll, in the stomach; Butter, Lautler, Kämpf, in the intestines; Stoll (later), Laennec, Paldamus, in the diaphragm; Strack in the cervical and tracheal glands; Armstrong, Astruc, in the larynx and esophagus; Whatt, Badham, Marcus, in the trachea and bronchi; Rossbach in the bronchi; Beau, Gendrin, Parrot, Wannebroucq, in the subglottic region;—it is clear that all these observers thought that the source of the paroxysm was in the peripheral distribution of the vagus. More recent writers, however, under the influence of the investigations of Rosenthal, Nothnagel, and others, have applied themselves rather to the physiologic "cough area" (Hustenpunkte) for an explanation of the production of the pertussis paroxysm.

This limitation should appear to be sanctioned to a certain extent, as the experimental employment of the laryngoscope in whooping-cough by Gendrin and Beau (1856) in the first instance had disclosed the irritative process acting on the supposed "cough area" (Husten-stelle), and as also Herff believed that he saw the following in his own person: A moderate inflammatory hyperemia of the respiratory tract from the posterior nares to the bifurcation of the trachea throughout the entire course of the disease. This inflammation was most marked in the interarytenoid region, on the posterior wall of the larynx, between the vocal cords, and on the under surface of the epiglottis. Even in the stage of decline the hyperemia remained longest over these areas. During an individual paroxysm a pellet of mucus was observed upon the posterior surface of the larynx on a level with the glottis, and when this was removed by forcible expiration the attack ceased. Irri-

tation of the mucous membrane in the interarytenoid region during the intervals excited a violent cough; on the under surface of the epiglottis, an evident yet feebler attack; while other parts reacted at most with a slight fit of coughing.

The theory of the paroxysms seemed now to be settled, especially when other writers (Rehn, Meyer-Hüni) confirmed these anatomic and laryngoscopic discoveries. Even the hypothesis of the mucus which collects in the larynx and trachea, and is found in the region of the glottis as a causal factor, was considered. But, unfortunately, other physicians not less careful and trustworthy, like Storch and Rossbach, denied or, like Löry, claimed that they frequently failed to find any change in the laryngoscopic picture in whooping-cough patients.

Moreover, writers did not agree as to the seat of the inflammatory lesions in the larynx. Beau, Copland, Gendrin, Meyer-Hüni, placed it above the vocal cords, Löry found it usually, and Rehn regularly, below these, while Herff and R. Meyer described it as between them. In contradiction to the laryngoscopists must be added the complete failure of the modern local treatment in whooping-cough, which, in spite of the greatest care and many trials by specialists, has in the practice of the most enthusiastic children's physicians completely failed to justify itself (Hauser). Again, animal experimentation, introduced especially by Georges le Serrec de Kervily in 1888 under Richet's direction, has only shown the impossibility of producing a typical attack from either a normal or an inflamed mucous membrane; for the cough curves exhibited by le Serrec are decidedly not whooping-cough paroxysms. Finally, the theory of the peripheral excitation of the attack by irritation of certain parts of the mucous membrane is unsatisfactory, because, without creating new hypotheses in support of the theory, it is impossible to understand why characteristic paroxysms should not be seen in other patients with similar lesions.

The older writers may have had something of this idea when they referred the responsibility for the attack to a point higher up in the nerve tract, even to the origin of the vagus. Lentin, Hufeland, Kilian, Jahn, Schäffer, and Schneider seek the cause of the paroxysm in an inflammation of the vagus. Breschet, Jahn, and Autenrieth confirmed this hypothesis by postmortem findings, thus contradicting Albers, who found out of 47 cases, in 43 no lesion of the vagus, and in the remaining cases only cadaveric imbibition-hyperemia.

Romberg, Friedleben, and Guéneau de Mussy later insisted rather on an indirect irritation of the vagus through the diseased and swollen bronchial glands. Romberg affirmed that as the compression of the vagus, by enlargement of neighboring bronchial glands, as a result of inflammatory hyperplasia or tubercular disease, may lessen the energy

of the vagus, a simple irritation of the glands, or inflammation without hyperplasia, may increase the energy, and in this case it would be the recurrent branch especially that would show the effect, and probably by inducing a spasmodic glottis affection. Friedleben now took up the question and defended, from anatomic observations made postmortem, both possibilities as a cause of the nervous disturbance. He therefore differentiated spasmodic and paralytic whooping-cough according as the closure of the glottis was produced by spasm or paralysis. Guéneau de Mussy asserted that he found in many autopsies an enlargement of the glands on one or the other side, seldom on both sides, which was evident clinically to percussion over the manubrium sterni, and he believed the paroxysms to be caused by compression and consequent irritation of the vagus by this enlargement. In order to explain the appearance of the cough in paroxysms, Duncan affirmed that the turgescence of the bronchial glands occurred intermittently.

But soon afterward F. O. Bara and Dolan denied the constant occurrence of this lymph-gland swelling, and thereby destroyed the theory built upon it.

Copland, Sanders, and Pidduck placed the anatomic seat of whooping-cough in the spinal cord. Copland found in every case an inflammatory irritation of the medulla oblongata and its membrane, while Pidduck in confirming the observations of Sanders endeavored to demonstrate a hyperemia of the vagus and other respiratory nerves at their origin, together with a profuse exudation of serum around the medulla oblongata (Biermer). Rossbach, on purely theoretic grounds, asserted an increase in the energy-producing power of the cough center in the spinal cord as an explanation.

J. Webster first located the seat of the disease in the brain. He considered whooping-cough a symptom of disease of the respiratory nervous system, and directed attention to the frequent complication of it with other diseases of the brain, especially hydrocephalus. Desruelles had a similar opinion, as he designated the disease by the name "broncho-céphalite": "Tant que la bronchite est simple, la toux n'offre rien de particulier, mais lorsque le diaphragme, les muscles expirateurs, ceux de la glotte, du larynx, la membrane postérieure des bronches, les vésicules aëriennes des poumons et même la voile du palais, suivant Laënnec, entrent en action, sont unis spasmodiquement sous l'influence de l'irritation cérébrale, la toux change de caractère; elle devient convulsive."

Lentin and others, especially Schönlein, sought the cause of the pertussis paroxysm in an injury of the centrifugal tract,—namely, the phrenic nerve,—while Laennec explained the disease as a rheumatism of the diaphragm.

A similar idea may have been in the minds of the older writers when they compared whooping-cough with epilepsy, the seat of which had been located in the brain since the time of Nicolaus Piso and Thomas Willis. Kilian designated whooping-cough an epilepsia pulmonum, and Jahn an epilepsia diaphragmatis, in the same sense that van Helmont and Selle spoke of a caducum pulmonum and de Haen named asthma an epilepsy of the lungs. The aura, the irresistibility of the attack, the participation of all motor and secretory organs, the loss of consciousness, the eventual general depression, justified the comparison, which strikes us as not very extravagant when we read that Willis observed in one case paroxysms of whooping-cough alternate with those of epilepsy. The observations of Whatt and Brodhurst, in which, according to Gibb, epilepsy occurred as a sequela in four cases, are less to be trusted.

Yet eventually we must regard as of the same value all opinions that are based on theoretic grounds or badly established facts. Consequently after the different and contradictory conclusions so far arrived at by clinical, anatomic, and experimental investigations, we can only confess our complete ignorance as to the cause of the paroxysm of whooping-cough.

An undoubted advance in this regard can be made only if renewed anatomic researches be undertaken by careful anatomists without dependence on old observations; if repeated clinical investigations, free from the prejudice of earlier hypotheses, endeavor to explain the attack and its symptoms according to the methods of modern neurology; if in all studies on the question the possibility be *à priori* conceded and remembered that the original localization of the epidemic disease may be different from the seat of the later symptoms—namely, the paroxysms. For the present general opinion that the catarrhal condition of the respiratory tract in the first stage is the expression of the original localization of the disease virus, and that the convulsive stage is caused by the persistence of the primary local infection, is only a hypothesis devoid of proof. As Josef Franck has insisted, whooping-cough has at its commencement too much similarity with the acute exanthemata to refer it entirely to a simple local infection of the mucous membrane of the larynx or trachea, and in the second stage it manifests a too marked dissimilarity with the symptoms of a chronic affection of the mucous membrane to regard such a hypothesis as explaining the pathogenesis of the disease.

PROGNOSIS.

ALTHOUGH, with respect to danger to life in our day, we regard the prognosis of whooping-cough as generally favorable so long as the malady remains uncomplicated, we are thoroughly aware that this applies only to the mild epidemics of the last few years, and that, as has been experienced in influenza, there is no certainty that epidemics may not change their character. The older writers, like Stoll, Danz, and others, dreaded whooping-cough more than smallpox, and the mortality of earlier epidemics is indeed sufficiently terrifying to make such a dread intelligible. If the cough epidemics in Rome in 1580 and 1630 were truly pertussis, the disease must then have raged violently, for in 1580 it claimed 9000, and in 1630, 20,000, victims. The fact stated by Rosenstein, that between 1749 and 1764, 43,393 children, or an average of 2893 a year, succumbed to the disease in Sweden, has been mentioned before; and it may be added that in the year 1755 alone, 5832 children were carried off by this disease. These figures are shown in their proper relation by the statement that from 1774 to 1795 only 7383 died from the disease, or an average of about 360 a year. According to Holdefreund, in Prussian Silesia from 1775 to 1780, 6617 succumbed, or an average of 1500 a year. Yet in a severe epidemic at Utrecht in 1777 van Tricht reports that in 80 cases there was scarcely one death.

In general, the epidemics on the northern and southern coasts of Europe have been more severe than those in the interior. Season likewise shows an influence on the mortality, inasmuch as mildly running epidemics may become severe with the appearance of damp, cold weather. In this regard Hufeland observed in Weimar after a rainy, cool summer, first measles, then scarlet fever, and finally whooping-cough break out. The last at its commencement showed a slight mortality and short course, but from the approach of winter onward there appeared frequent pneumonias with numerous deaths, and on the return of spring the malady assumed a chronic but favorable character.

Age in prognosis *quoad vitam* is of undoubted significance. Children under three, and especially nurslings, are in great danger, while with increasing years the mortality decreases more markedly even than the morbidity.

According to some writers, strong, plethoric children, on account of their inclination to bronchitis and pneumonia, are more imperiled than their weaker brethren. Complication with scrofula, rachitis, and tuberculosis aggravates the prognosis much more than the occurrence of measles or smallpox, while scarlet fever has even a less unfavorable influence on its course. That attacks of impetigo, scabies, tinea capitis, and smallpox ameliorate the course of whooping-cough when they occur at the same time, and that they will protect from it when they occur previously, is—contrary to Hufeland, Schönlein, and others—disputed rather than confirmed by the majority of authorities.

In individual cases it must be regarded as favorable when the transition into the convulsive stage occurs slowly. The longer the time before the whooping inspiration announces its commencement, the milder, as a rule, is the course. The more absolute the interval—that is, the more exempt it is from prostration, melancholy, or other sign of disease—the better the prognosis. The fact that the attacks are becoming less frequent or milder before a certain time, is not always of favorable import. At least, in the second and third weeks it points to beginning inflammation. Marcus reports sudden cessation of the cough immediately preceding inflammation of the lungs. Violent and numerous attacks are to be feared on account of the eventual exhaustion of the patient.

Every inflammatory complication aggravates the danger, and the more so, the younger the patient. In fact, pulmonary inflammations are in a special degree the chief factor in the mortality of whooping-cough. The mechanically produced complications damage the prognosis, inasmuch as they occur in important organs and hinder essential functions. Profuse hemorrhages from the nose, bronchi, etc., are dangerous on account of the subsequent anemia (Huxham); purpura as an expression of previously existing cachexia, or of one produced by profuse bleeding, is always a *signum mali ominis.* Uncontrollable vomiting, spasm of the glottis, and subcutaneous emphysema are among the most serious complications. The occurrence of eclampsia is almost always of fatal import. Of 10 eclampsia cases, 9 will die in whooping-cough, and the rare one that lives will commonly show incurable traces in the form of paralysis, contractures, etc. Yet we must not omit that, according to Friedrich Hoffmann and Josef Franck, the appearance of convulsions is often a sign of a favorable change in the disease.

Stoll observed whooping-cough disappear with "rheumatic pains in the neck" ("rheumatischen Nackenschmerz"). According to Hufe-

land, strangury in a late stage promises recovery. According to Kopp, moderate vomiting is good. Naturally, not much reliance is to be placed on these and similar prognostications.

That a severe case often becomes rapidly better with the setting-in of mild weather, may be taken as well established.

In reference to complete recovery, it is to be remembered that Rosenstein, Morris, and Josef Franck saw children who seemingly recovered in the autumn, attacked again the following spring, as if the disease had in the mean time lain dormant.

The most serious sequelæ, scrofula, tuberculosis, and nervous disease, depend more on the constitution and heredity of the patient than on the whooping-cough itself. It is scarcely in the province of prognosis to define how much may remain of mechanically produced complications.

Finally, we may add that treatment by an ignorant physician aggravates, that by an experienced one improves, the prognosis.

TREATMENT.

Since whooping-cough, in the very great majority of cases, is spread by contagion, and only rarely miasmatically (and then under conditions impossible to foresee), the first essential in *prophylaxis* is the avoidance of contact with whooping-cough patients.

"Unica prophylaxis consistit in fuga contagii; summa quoque supellectilis et vestium infectarum ratio habenda est" (J. Franck).

And it is true that even in the presence of a wide-spread epidemic children have often been protected from the disease by parents who were careful as to their contact with others, until they had passed the dangerous age. Yet in general such protection is impossible. And accordingly it is not uncommon for intelligent physicians and parents to regard it a duty in whooping-cough, as in other contagious diseases, not to isolate the children too carefully in mild epidemics, but rather to leave them exposed, especially if a brother or sister has already been attacked, so that they may be immune in case of a more severe outbreak in the future. Still, this does not apply to very young children, or to any child who appears predisposed by heredity, constitution, or previous diseases to a severe course; on the contrary, children under four years, or of consumptive parents, or scrofulous and rachitic children, and those affected at the time with measles, must be protected in every possible way from contagion. It is, moreover, advisable to take into consideration the season in which experience has shown that the serious inflammatory complications occur most frequently—namely, the end of winter and autumn.

Schools, play-grounds, kindergartens, and shelters are most commonly the foci from which the contagion spreads. In severe epidemics these must be closed if prophylaxis is to remain no empty word.

Although the greatest risk of contagion is during the catarrhal stage, and although the patient at the height of the convulsive stage, is seldom dangerous, it may be taken as a rule that the person is to be avoided as long as he coughs. On this account it often becomes difficult for the physician to carry out one of the measures recommended in treatment to be mentioned hereafter—namely, change of climate; for the contamination of a place hitherto free from whooping-cough is a responsibility that neither physician nor patient should take on himself without much consideration. The love of our neighbor should

make it decidedly our duty to keep the patient at a distance from sus-
ceptible individuals. The—at most very slight—danger of taking the
disease a second time makes caution superfluous in regard to adults
and children who have had the disease.

If the removal of the sputa and excretory matter generally, of the
patient's linen, etc., away from contact with individuals in families and
schools was demanded as a strict essential for cleanliness and refine-
ment in non-contagious as well as contagious diseases, there would be
no question as to whether such measures were necessary in individual
cases or not. In whooping-cough this rule should be put in force
independent of every theory of the disease. Disinfectants are super-
fluous in pertussis, and are to be avoided all the more because their
introduction leads to natural laziness and inattention, for human
nature appeals gladly to the careful employment of incantation and
ceremonies in order to get rid of the simplest duties.

According to Monti, Mohn, of Norway, insists that he has repeatedly
cut short whooping-cough by a thorough disinfection of the room in
which the patient lives with sulphurous acid. Bed, clothing, linen, play-
toys, in short, everything with which the patient came in contact, were
fumigated for six hours with sulphurous acid, for which 25 gm. of sulphur
were reckoned for every cubic meter. The room was then aired, the
patient covered with fresh linen, and put to bed. The next day showed
the disease to have disappeared. This satisfactory report was confirmed
by Schönberg in Christiania.

Since at the time of an epidemic every cold makes the individual
more susceptible to the disease, protection from catching cold, as
insisted on by many practitioners, is an important part of the prophy-
laxis.

Preventive measures against whooping-cough are at present lack-
ing. True, Hahnemann recommended as such the tinctura seminis
santonici, and others belladonna or vaccination. But, unfortunately,
Jahn's words apply to-day: "No dietetic precaution, no purification
or strengthening by internal or external remedies, no adjunct, can be
mentioned which will prevent whooping-cough, if it is necessary to
remain within the limits of the epidemic and of the contagium." To
seek a means of protection is not at all unreasonable. The favorable
experiences reported by Italian physicians as to the prophylactic effect
of salicylic acid in epidemics of measles are not improbable, if I may
be allowed to form a conclusion after a dozen trials.

An individual being attacked, the first question is: Is there any
means by which the disease may be cured, shortened, or its course
made milder?

Writers are very divided in their opinions on this matter. While some, and these not the most ignorant, agree with de Baillou that whooping-cough is an incurable disease, and, in opposition to the curing (sanare), insist on the importance of nursing (curare), others look to definite remedies, specifics, and abortives to save the life and bring about the recovery of the patient. In contrast to the rule of the South German peasant, that whooping-cough "continues till it stops" ("so lange dauert, bis er aufhört"), stands the assurance of enthusiasts that they are able to cure the disease in the shortest possible time.

Quite recently the conception of a specific as applied to whooping-cough has been narrowed down so as to signify an abortive. Our predecessors had, besides a careful diet arranged to its smallest details, some one or other favorite remedy which might aptly be compared to the carrying of an amulet alongside a pistol on a dangerous journey, or to the little follies of a great man which proclaim his human origin. Cleverness naturally paid the greatest attention to this favorite remedy, while overlooking the most important part of the teaching of the master. Therefore it happened that Thomas Willis, besides emetics and purgatives, recommended most highly muscus pyxidatus as a cure for whooping-cough; Ludovicus Mercatus, "ferrum candens" [the actual cautery], or a tuft of hair on the back of the head; Ettmüller, liquor cornu cervi succinati; Sydenham, venesection and vesication; Friedrich Hoffmann, clysters, electuaries, and diaphoretics; Astruc, emetics and venesection. And it was reckoned wonderful when Rosén v. Rosenstein employed three specifics, one after another: Rosmarinus sylvestris, found by Linné in use among the people as a specific against the "insects" of the whooping-cough miasm; the fat of Phoca vitulina against the convulsive attack, which was cured in eight days by the administration of broken doses of one-half ounce of this boiled with a pint of milk; and, finally, a mixture of tar and the yolks of eggs to remove any remaining catarrhal cough. Werlhof, with his syrupus coralliæ and spiritus salis dulcis; Huxham, with his venesection and mercury; Strandberg, with his arcanum tartari; Sauvages, with his sugar of lead,—all these found even enthusiastic followers and confirmers, just as de Haen did, when he gave out kermes mineral as a specific in the epidemic from 1747 to 1750, but condemned it as useless in 1751, and vaunted as remedial instead garden snails cooked in beer or milk and earth-worms in an aromatic decoction. Moreover, Morris became famous through the employment of Peruvian bark (which had been recommended by Brendel, Strandberg, Forbes, and Weber) in combination with castoreum, and his fame increased when he assured a complete cure in eight days by the inhalation of the disgusting emanation from a goat or a fox. After this Millar recommended asafetida; Gesner, musk and extract of tobacco; Brandt, the fat of seals; and Buchan found followers when he proposed rubbing the soles of the feet night and morning with garlic and pork fat, like Löbel von Löbelstein when he put his salve of camphor and phosphorus on the abdomen.

The most intelligent physicians of every age pursued these and similar trifles with a seriousness equaled only by our present-day lesser lights, who proclaim their specifics under grandiose names that bear no con-

tradition: "Tussol" and "Pertussol," "Pertussin" and "Antispasmin" and "Convulsin," should impose no more on the physician of to-day than would the ridiculous muscus pyxidatus, the decoction of earth-worms, or the stink of the goat.

Modern names frequently conceal the revival of old remedies. So, for instance, pertussin is the "extractum thymi saccharatum," and the English swindle, "Roche's Embrocation for the Hooping-cough," at five shillings a bottle, is only a capricious and unstable compound of asafetida or opium and turpentine. Here and there it is considered to contain, besides, an infusion of dried wood-lice.

Many physicians, under the delusion of being scientific, direct their treatment in whooping-cough, as in other diseases, too much in accordance with the theory in vogue as to the nature and seat of the disease, instead of depending on experience, which is the only criterion.

And so, one takes to the resolvents, from sal ammoniac to kermes mineral and the golden sulphuret of antimony; a second to evacuants, from purgatives to emetics, from the seton to the pustule salve; a third to emollients, the mucilages, and oils; a fourth to antispasmodics, valerian, asafetida, chamomile, musk, zinc oxid; a fifth to narcotics, belladonna, opium, morphin, hyoscyamus, chloroform, chloral hydrate, bromid; a sixth to anticatarrhals, the alkalies and astringents; a seventh to tonics, quinin, arsenic; an eighth to antizymotics and antiseptics, sulphuric acid, iodin, carbolic acid, benzine, and illuminating gas; a ninth, finally, to psychic therapy, threats, blows, a push from a step (Cullen), and other asinine means.

And what one recommended, the other rejected, till finally a glance over the history of whooping-cough therapy makes us confess with Heberden: "Multa quidem ubique jactantur hujus pestis remedia, ut fieri solet adversus morbos, quorum nulla certa remedia inventa sunt. De talibus auxiliis vetus illud nimis verum est: ὦ φιλοί, οὐδεις φίλος!"

Yet a few things may be rescued from this stream with profit, for, though they effect no wonders in the disease, they can, in intelligent hands, be made to influence its course. Among these we will mention, first, certain drugs which have come to us strongly recommended, which may be readily tested by any physician, and which possess for the theorists the advantage that their use opposes in no way the hypothesis of a miasm or contagium vivum.

In the first place stands quinin, which owes to Binz its general reputation and proper employment.

We have already mentioned that a few physicians in the middle of the eighteenth century—Brendel, Strandberg, Forbes—recommended Peruvian bark in whooping-cough. But they gave no definite indications for its employment. It was only that the panacea quinin ought to cure whooping-cough also. Later physicians, like Paldamus, Danz, and Hufeland, expressed their opinion that it was most efficacious in the disease, but they raised a warning against the employment of it too early

in the case. Götz commended the antitypical effect of quinin in an epidemic showing intermittent attacks in 1866. The first intelligent recommendation of quinin hydrochlorid as a remedy that would shorten the course of whooping-cough was made by Binz, who took it up from a theoretic consideration of the nature of the disease, and the physiologic action of the drug, but finding that the empiric results corresponded with the theory, he gave it to the world as a remedy. His communication, and the dissertation of his pupil Jansen, were followed by confirmations from Breidenbach, Steffen, Rindfleisch, Keating, Rassmund, Hesse, Hagenbach, Laubinger, and others, all of whom agreed as to the considerable shortening of the course, and the marked diminution in violence of the attacks brought about by the treatment. That some have rejected quinin without testing it, or after employing it incorrectly, or without result on account of the neglect of the nurse, is not to be wondered at.

From the beginning Binz advised the administration of the remedy in large doses: The child should take at least as many decigrams of quinin hydrochlorid three times daily as it is years old, or as many centigrams as it is months old. If the simple hydrochloric acid solution with a corrective is rejected on account of its bitter taste, the physician should spare no trouble in order to show the relatives or those in charge of the patient how to make it palatable, or how to conceal tablets or pills in sugar or fruit juice. No one need be surprised at his failure in children's practice if from high Olympus he writes his prescription for quinin, and hurries away saying: "Now see to it that he gets his medicine. I have something more important to do." In case of necessity the quinin may be administered in enemata, as Rindfleisch gave it to his own children, or in suppositories, as Pick advises. At von Noorden's request, small gelatin pearls and chocolate tablets have been put on the market containing one decigram of quinin hydrochlorid, the taste of which has been entirely concealed. These are certainly to be recommended for the children of opulent parents. Yet the physician will usually find that children, especially the very young ones, are not so sensitive to the taste of quinin as adults, and that the difficulty in administration proceeds not so much from the child as from the physician who carefully warns about the taste, and ·from the parents who preface the administration with: "You poor child—to have to take such bitter medicine." Whoever feels regard for his own and strangers' children must realize that toward them there should be only a categoric imperative: "You must, since you shall, and you shall since you can!" Yet naturally there are gentle and rough ways of accomplishing the same thing.

On account of this greater solubility, quinin hydrochlorid is to be preferred to the sulphate. The (non-official) tasteless tannate of qui-

nin must be given in at least three times larger doses, since it contains usually less than 25% of quinin, while the hydrochlorid contains 83%.

The earlier the treatment is begun, the sooner may we expect the termination of the disease. As far as the result is concerned, age makes no particular difference.

O. Hauser's advice is worthy of consideration—namely, to give the drug always after a paroxysm, since then the danger of exciting a new attack, or of causing vomiting, which would make the administration useless, is least. The introduction of the quinin at any price by a stomach-tube or subcutaneous injection, as recommended in certain Inaugural Dissertations, is cruel torture, approved by but few and carried out by none.

The injurious effects of quinin are in any case no greater in children than in adults. Injuries to hearing, sight, and the digestive apparatus have been reported by some who oppose the employment of quinin in whooping-cough, but from their communications it was impossible to judge if they realized the similar effects that whooping-cough itself might produce, and had differentiated them from the effects of the quinin.

After quinin, a second drug deserves mention as a remedy in shortening the disease—namely, camphor. Since Max Jacobi, in 1804, recommended it in doses of from 0.5 to 2.0 gm. daily, and affirmed that it converted pertussis into a mild catarrh in ten to twelve days, it has been sometimes lauded and again thrown aside. Personal experience with children who required a strong restorative on account of complication-bronchitis and increasing exhaustion has convinced us as to its beneficial effect on the course of the disease. Moreover, in the face of only a few observations we dare affirm that we believe it efficacious, not only through the digestive tract, but even through the external auditory meatus. These observations have been, unfortunately, exaggerated by a suspended "Collegen" for the purpose of swindling, and have been criticized, not without prejudice, by Josef Keller in his Dissertation. It is unnecessary to mention here chinolin and its derivatives and chinoidin. We will likewise pass over phenazone (antipyrin), acetanilid, and phenacetin, though they have been recommended. Their effect is not so favorable as quinin, and their use is frequently accompanied by such serious danger to children that there appears to be no reason to consider them further.

Whether the physician takes to the "specifics" or not, he is at least obliged to so regulate the dietetic treatment of the patient that no danger is incurred from this side. The first statement of Josef Franck,

"tussis convulsiva simplex secundum statum scientiæ nostræ hodiernum optime curatur, dum fere naturæ committitur," may be denied; but his other statement should not be neglected frivolously: "Officium medici in eo consistere debet, ut regimen diateticum huic morbo consentaneum præscribat, ut symptomata, quoad usque fieri licet, leniat, utque vigilet, ne alienus morbus sese insinuet."

The dietetic treatment of whooping-cough patients is the natural one pertaining to such a disease, its complications and special dangers. It varies with the stage of the disease, the character of the epidemic, and the constitution of the patient.

The danger of inflammatory complications is insisted on by all writers. Moreover, they agree that this is greatest in the catarrhal stage and the second half of the spasmodic stage; and that in the former the character of the epidemic, in the latter the general constitution of the patient, is responsible for these complications. Yet all allow that "catching cold" is a most important auxiliary cause. And although of late years this designation has been ridiculed as unscientific, the endeavors to place it on a more scientific basis have not only been fruitless, but Samuel's experimental investigations have added such significant facts in regard to it that it seems best to allow it to remain.

Therefore, a well-regulated and temperate climate is to be sought in every stage where there is danger, in order to protect the child from inflammations of the respiratory tract. If the weather without is moderately warm and moist, there is no objection to open-air treatment. Temperatures under 65° F. make an artificial room-temperature necessary, and the more so if the outside air is damp and in any sort of violent movement. The cold, dry northeast wind, and the rough north wind are feared in Germany, not without reason. In cold damp weather the air of the room should be dry, but not over 75° F.; for if it is too warm, it increases the irritability of the respiratory tract and induces general torpidity. Intense heat outside is injurious only in proportion to its effect on a particular patient. The infrequency of whooping-cough in the tropics and its mild course below temperate degrees of latitude make the heat of the sun more desirable than absolutely beneficial; for, although some have observed that children cough more in the shade than in the sun, others assure us to the contrary. Yet all agree that *cæteris paribus* the open air is to be preferred to the room as soon as the catarrhal stage has passed and an uncomplicated convulsive stage set in. Ullmann, after carefully observing the influence of indoor and open-air treatment, found that on an aver-

age the interval between paroxysms was three times as long under the latter in comparison with the former.   It is unnecessary to mention that the morning and evening fluctuations of temperature are to be avoided.

The protection of patients from injurious temperatures and winds is no more important than their protection from impure air.   Scarcely any one doubts that smoke and dust, and every sharp and irritating vapor, tend to increase the paroxysms and make complications more likely, and only the blindest search after an antizymotic specific could advise the vaporization of chlorin in the patient's room, and similar short-sighted measures.   Intelligent physicians consider that the paroxysms may be increased by the accumulation of carbonic dioxid due to the residence of many people in the room, insufficient ventilation, or the keeping of plants in it at night-time, and this has been made probable by the inhalation experiments with different gases carried out by Haucke in whooping-cough.   The presence of plants in the room during the day, in order to absorb the carbonic dioxid has been recommended by several writers.

Special attention should be paid to the clothing of patients, since irritation of the skin may increase the paroxysms.   Yet an unreasonable excess of clothing, the wearing of tight or heavy garments, to which so many people resort in order to prevent cooling of the skin, are to be avoided.

It is remarkable how many hoods and raiments, clothes, skirts and underskirts, waist-binders, shirts and undershirts, must be removed before the little pertussis patient comes into view, and, to say the least, it is always a surprise that the little one can breathe or cough at all.   Thin loose flannel drawers for the buttocks and thighs over or under a shirt, a moderately tight waist, for children with weak abdominal walls a simple belly-band, wool or cotton-wool stockings, and the simple clothes made out of light or heavy stuff, according to the season, are sufficient during the day to retain the body-heat and shut out the cold.   At night, besides a shirt and a long gown reaching beyond the feet, children who are subject to frequent attacks, or are accustomed to throw off the bed-clothes, should have a light flannel or *tricot* overgown.   Yet it is to be remembered that often the so-called naughtiness of children in kicking the bed-clothes off is attributable to too warm or heavy covering, or to neglect in fastening the bedclothes.

Every mother surely knows that the bed must be warm before the pertussis patient is put into it.   She takes care, too, that the room-temperature is not under 60° or 55° F., but likewise not over 65° F.

The slightest bronchitis, like the most severe bronchopneumonia, requires continuous rest in bed. And the smallest rise of temperature is to be treated in the same way.

Exercise and rest are quite as necessary to the pertussis patient as to the healthy. In an uncomplicated case these may be regulated by the patient's own instinct. The appearance of complications, or accidental diseases, and a greater frequency of the paroxysms, call, naturally, for more rest.

In the catarrhal stage food and drink are to be chosen with attention to any fever present, and to the catarrh. All exciting, stimulating nourishment, all luxuries, are to be avoided especially in the convulsive stage. Everything that irritates the sense of taste, the esophagus, larynx, or stomach may excite cough, and Vogel's warning against dry bread and cake on account of the possibility of crumbs lodging in the throat is worthy of notice. Overfilling of the stomach during the spasmodic stage provokes cough and vomiting, yet undernourishment must be avoided. Consequently, the frequent administration of small amounts of concentrated nourishment seems rational, and experiment has proved it. Milk gruels of oatmeal, rice, barley, and sago; egg foods; ragout of chicken; boiled or roasted beef; boiled or stewed fish; white bread or biscuit (rusk) broken down in milk; and preparations of malt, are the foods on which pertussis children seem to thrive best. It must be decided in individual cases whether liquid or solid food is to be preferred. Trousseau may be correct in holding that solid food is more easily digested and absorbed in pertussis than liquid; yet children in the first years of life must live on milk diet, and a physician ought not, without good reason, to advise its discontinuance at any age, but rather allow it without limit. The opinion of nurses that milk causes a deposit on a mucous surface that obstructs secretion, and is therefore to be avoided in catarrh, is incorrect, and originated in the fact that milk coats the tongue and buccal cavity of adults and children suffering from digestive disturbances. The addition of lime-water to the milk usually does away with this, and the same or a little table salt will aid in preventing too rapid a coauglation of the milk in the stomach. Broths are sometimes well borne by feeble children, and even by sucklings, acting as an excellent and rapidly working restorative. Given in proper proportion and with care, they produce no ill effects, and completely replace alcoholic drinks, employed too generally for children. If the last are exceptionally indicated, an old Rhine wine or an unadulterated mild southern wine is to be recommended. The so-called children's wines, Tokay and others,

any mother can prepare better and cheaper with a little sugar and a few drops of Rhine wine; though it is better to avoid them.

[Should the stomach prove irritable, a suitable meal will be equal parts of whey and egg-water. There are several varieties of whey, according to its mode of preparation: for example, ordinary two-milk whey, prepared by adding one part of fresh buttermilk to two parts of warmed milk; alum whey, prepared by turning warmed milk with powdered alum in the proportion of a quarter of an ounce to a pint (astringent); rennet whey, made by curdling warm milk with essence of "rennet," which is the mucous membrane lining the fourth or digesting stomach of the calf; tamarind whey, made by stirring two tablespoonfuls of tamarind into a pint of milk whilst boiling (laxative); and white wine whey, made by adding a wineglassful of sherry to half a pint of warmed milk and straining (stimulant). Egg-water—the *eau albumineuse* of the French—is prepared by whipping up the whites of two, three, or four eggs to a foam, then stirring the froth into a pint of cold water and straining. This albumin-water replaces the casein of the milk which has been separated as indigestible curd in the making of the whey.]

The rejection of food on account of fear of a paroxysm, as occasionally seen, must be combated with kindness and strictness before resorting to the extreme measures of enemata and the stomach-tube.

We do not believe that any specially arranged diet can cure the disease, yet we wish to mention that others have claimed this. For instance, Hannon reports cures in every case in fourteen days, occasionally even thirty-eight days, by a tonic diet ("tonisirende Ernährung"). He gives in the morning roast meat, with toast, and pure Madeira or port wine; at noon, biscuit with wine; in the afternoon, meat broth, roast meat, toast, and wine; in the evening, wine; at night, cold water; no milk, no vegetables, no soup, no puddings.

It is scarcely necessary to mention that every disturbance of excretion requires prompt attention. It is not prejudice to say that constipation may cause an increase in paroxysms, an elevation of the body-temperature, cerebral congestion, and even an outbreak of convulsions. An enema, a suppository, or a small dose of calomel is usually sufficient. Enfeebling diarrhea, which occasionally occurs in whooping-cough, must be met in time with renewed diet regulations and the administration of antidiarrhetics proper to the age.

As individual indications in the dietetic management of whooping-cough the following must be mentioned in addition:

Attention to predisposition and heredity may show special indica-

tions, especially in the spasmodic stage and during convalescence; for instance, rachitic and tubercular children should be sent to the country, seashore, or woods, and be given salt baths. The administration of calcium salts or iron (especially the easily absorbed tinctura ferri pomata, of the German Pharmacopœia, or the tinctura ferri acetici and chloridi ætherea) or preparations of quinin is indicated.

It is natural that in an epidemic or during a season which shows more than its proportion of inflammatory symptoms all prophylactic measures for preventing the disease or ameliorating its course should be carried out with especial rigor.

In the after-treatment measures to build up the strength are called for, in the form of easily assimilable food, nitrogenous preparations gradually increased, malt extracts, cod-liver oil, and tonic drugs, as decoctions of cinchona or calumba, iron, and (exceptionally) small quantities of good wine. Yet the best tonics are, besides an ordinary diet, fresh air and moderate exercise.

Special emphasis must be laid on the *symptomatic treatment.* This is to be carried out on the principle that every symptom should be combated if it threatens danger, but left to nature if it can be borne without disadvantage.

In the catarrhal stage, an excessive inflammation is to be feared. The slightest symptom of beginning bronchitis is an appeal for active interference. The danger of catarrhal pneumonia, especially in strong, full-blooded children, calls for the immediate administration of an emetic on a rise of temperature. Tartar emetic in the form of antimonial wine, a teaspoonful every ten minutes till it acts, is usually sufficient for children under two or three years of age. For older children, over five or six, Hufeland's "linctus emeticus" may be chosen:

R. Powdered ipecacuanha 1.5
    Tartar emetic 0.03
    Oxymel of squill   } of each................20.0
    Syrup of raspberries, }
    Distilled water ....40.0   M.
  Sig.—One teaspoonful every fifteen minutes (adults, one tablespoonful) till
    vomiting occurs.

or apomorphin hydrochlorid 0.5 to 1.5 milligrams subcutaneously.

It is scarcely necessary to mention that, before the emetic is given, the intestine should be emptied by an enema, and the emetic itself should be aided by subsequent drafts of warm water.

In less pressing cases the emetic may be replaced by an expecto-

rant given in nauseating doses. The most serviceable for this are preparations of antimony, especially Plummer's powder,* ipecacuanha (0.2 to 0.3 radic. ipecac. : 100.0 as infus., one teaspoonful every two hours; or vinum ipecac., 10 to 20 gtt. several times), or flores benzoës (0.01 to 0.03 every two hours).

For feeble children the liquor ammonii anisatus or camphor with or without benzoin may be advisable.

As simple auxiliary expectorants in whooping-cough, the "species pectorales" and the mild Ems and Seltzer waters are recommended. These mineral waters are taken after the addition of sugar (to expel the CO_2) or in hot milk. They are useful, too, in a spasmodic stage as a night-drink and as a means toward soothing the cough.

["Species pectorales," a preparation of the German Pharmacopœia, called "Brust-Thee" (chest-tea) in the vernacular. It is composed of marshmallow root 8, licorice root 3, orris root 1, coltsfoot leaves 4, verbascum flowers 2, all coarsely cut and mixed with crushed aniseed 2.—J. Oldham Braithwaite.]

That the opposite of alkalies—namely, acids, and especially mineral acids—have been recommended as efficacious in whooping-cough occasions no surprise when we consider the freedom of the science of medicine. Yet we would not like to stand responsible for the recommendation of nitric acid (Arnoldi and Gibb) and hydrochloric acid (Thiel, Henke, West) in the catarrhal stage.

In the spasmodic stage of uncomplicated whooping-cough, we must first take up the paroxysm. When we consider how much the patient suffers during the paroxysm, and how lastingly injurious this is to his whole system, we must realize what would be accomplished if we could combat this symptom. For no one would have the temerity to affirm that it was a salutary reaction of defense on the part of the organism which it would be dangerous to suppress. It belongs to the category of futile efforts on the part of the respiratory apparatus, of which Lommius says: "Omnis tussis mala, qua somnus aufertur; inutilis etiam, quæ longo tempore frequens gravisque hominem exercet."

There is no specific for the prevention of the paroxysm. For although it is true that we possess effective means to mitigate it, it is likewise certain that at any juncture they may all fail, so that the physician must know several remedies from which to choose in case

* ℞.   Stibii sulphur. aurant.,⎫ .... aa 0.01
       Calomelanos,   ⎭
       Sacchari albi .... 0.2.
M. f. p. Dnt. tal. dos. No. x.
Sɪɢ.—One powder every two or three hours.

of need. The proper combination of these palliatives will therefore differ in individual cases.

Certain physicians have very highly recommended for the paroxysm psychic or suggestive therapy in the form of commands, threats, and punishment.

Willis long ago said: "Subito quodam timore afficiantur (scil. ægroti); hinc cum medicamenta minus efficiant, apud vulgus in praxi familiare est, ut pro terriculamento, dum molendium ingens cum stridore et rotarum aspectu horribili circumagitur, affectus grani sive frumenti receptaculo imponatur indeque morbi hujus subita curatio nonnunquam contingit."

Better known is the remark of Felix Niemeyer: "I have heard the wife of a Prussian general, who was a resolute though tender mother, say that whooping-cough could be cured only with the rod. This conclusion, and the general advice to exhort—that is, to force—children to struggle against the cough, gave offense here and there, and even brought down public indignation. Yet, supported by personal experience and the confirmation of intelligent physicians, I must repeat this advice with marked emphasis. In the case of rough and ignorant parents, it is naturally not suitable."

What some awaited from psychic treatment, others sought in change of air and climate. This advice seems to have originated with Heberden: "Usu didicimus mutationem cœli maxime valere ad vim morbi leniendam et finem ejus accelerandum." Some insist on repeated changes of air when the attacks do not lessen in frequency and intensity in a short time. Every experienced physician realizes the efficaciousness of this measure. Samuel Merriman (in "Underwood's Manual") and others after him carry their skepticism too far when they affirm that they saw no single case at the height of the disease improve on change of air; and add that a mild climate is beneficial only during convalescence. We mentioned previously the moral ground that underlies the question of change of climate.

As palliatives for the paroxysm we will consider first special drugs. Those recommended are so numerous that we will take up only the authenticated ones. From the time of Schäffer up to some years ago, the most used and most highly valued remedy in Germany was belladonna.

Trousseau's recommendation in France gave it a new reputation. Innumerable authorities approved it, while but few opposed it. And although it merits the greatest confidence, it has been unfortunately of late years replaced by morphin and opium, and many other drugs which are, however, worthless. It may be given as an infusion of the leaves, according to Jahn's original prescription (foliorum. bellad., 0.5

to 1.0 : 180, a teaspoonful every two or three hours till the appearance of faintness); or according to Trousseau's method, which provides for one daily dose to be taken while fasting, and repeated every two or three days increased in amount, keeping a sharp lookout for symptoms of poisoning. To children under four years Trousseau gave first 0.5 centigram pulv. radic. bellad.; to older children, double the amount. He later employed atropin; administering to a child first 0.25 milligram in the morning, then every two or three days till ten or twelve 0.25 milligram doses had been given. For violent vomiting after the attack, Trousseau gave ½ to 1 gtt. of the tincture of opium. Not only the old physicians, as Ettmüller and Frank, but recent ones, as Archambault, Meyer-Hüni, and Heubner, recommend belladonna or atropin.

Practitioners like Seifert, Curt Hübner, and others, order as many drops as the patient is years old to be given three times daily from a solution of 0.05 extr. bellad. in 10.0 mist. amygdal. amar.

Next to belladonna, opium or its alkaloid, morphin, is most highly recommended. At one time considered dangerous in children's practice, it is to-day, perhaps, sometimes prescribed too rashly. Vogel, who claims opium and morphin to be indispensable hypnotics in whooping-cough, warns against an extravagant or too long employment of them. The only writer who repudiated opium in pertussis was Stoll (caveat opio!), who, in his description and consideration of this disease, is peculiarly, and for this celebrated clinician astonishingly, obscure. According to Matthaei's old prescription, children under one year should be given ⅛ of a drop of the tincture every fifteen to thirty minutes, till the effect is produced; never more than one drop at intervals of from three to four hours. Children between five and ten years of age may receive one drop of the tincture of opium every two to three hours. Brown, Hufeland, and Vogler advise a combination of ipecacuanha with the opium, and recent physicians also have preferred Dover's pulvis ipecacuanhæ compositus. It is sometimes advisable in very susceptible children to administer with the opium some coffee or liquor ammonii anisatus, in combination with a small dose of atropin, in order to prevent dangerous or injurious effects. For patients with an inclination to cerebral congestion, experienced physicians prefer opium to morphin; and for pale anemic individuals, the reverse.

Although Starke and Hufeland asserted the extract of hyoscyamus to be a specific for the paroxysm, it never established itself in practice. The same is true of Cicuta virosa, Conium, Nicotiana, Musk, and Cas-

toreum, in spite of the recommendation of authoritative physicians. Moreover, many modern remedies, which it is unnecessary to enumerate here, will pass in the same way, not so much because they are absolutely useless as because they possess no advantage over belladonna and opium or produce bad effects that were at first concealed. This is probably true least of all for bromoform, recommended by Stepp, and given in the dose of two or more drops every six to eight hours in sweetened water. This replaced the chloroform inhalations recommended by Marley (1863), who gave them up a short time later. There is already in the literature a series of cases of bromoform-poisoning, although out of fourteen cases collected by Börger only one ended fatally.

[Misadventures with bromoform have occurred not infrequently, but may be easily avoided by care. They have usually depended on the fact that bromoform, being of very high specific gravity and but slightly soluble in water, is apt to fall to the bottom of a mixture. The density of this limpid, colorless, sweet liquid is 2.829 to 2.833 (Martindale). The "aqua bromoformi" is made by shaking one minim thoroughly with two ounces of water. Martindale suggests an emulsion under the form of a "mistura bromoformi" having the following composition:

Bromoform	½ fluidram
Tincture of senega............................	3½ drams
Syrup of orange.............................	½ ounce.

Shake and gradually add water to six ounces. Dose, 2 to 4 drams.

All risk may be avoided by thoroughly shaking any mixture containing bromoform just before the dose is measured, or by giving the remedy in capsules, each of which contains half a minim dissolved in oil.]

An intense blennorrhea, appearing not infrequently in the convulsive stage, especially in feeble scrofulous individuals, is best treated, according to Geigel, with tannin or a mixture of tannin and gum benzoin (0.01 to 0.03 āā every two or three hours), or with alum (0.1 three times daily in young children, 0.5 in older ones), as recommended by Golding Bird and Henry Davies. It is worthy of mention that with the use of the last Davies claims he never saw constipation, but rather diarrhea.

It is unnecessary to mention other remedies for the cough. Any one seeking others, can find old and new remedies in quantity in Biermer's manual, in the Dissertations of Sterling and Hochfeld, in the References of Vogel and Hagenbach, not to mention the fact that almost every new

number of the different weekly journals brings to light a new remedy recommended as most efficacious. Yet we desire to add that many physicians, becoming discontented with the results of internal medication or enticed by the theory of the localization of the disease in the upper air-passages, attempted to attack directly the hypothetic *locus morbi*, and thereby prevent the attacks.

Watson, Joubert, and especially Bouchut cauterized the throat with lunar caustic, and by daily applications cured the disease in from eight to ten days, though Vogel and others got no results from the method. Inhalations of tannin and opium were advised by Steffen, of potassium bromid by Helmke, of carbolic acid by Birch-Hirschfeld, of nitrate of silver by Rehn. Prior and Mugdan painted the throat with cocain with good results, Hagenbach and Henoch in vain, while Unruh found applications of the tincture of iodin or tannic acid to abort the disease.

After the treatment of the pharynx, larynx, and trachea had proved unsuccessful, the nose was attacked. Sommerbrodt cauterized it, Michel puffed quinin and boric acid and gum benzoin into it, Sonneberg antipyrin (phenazone), Strübing a powder composed of 1 part nitrate of silver and 9 parts magnesia usta. After carefully collecting the literature on these new methods, Barbot comes to the correct conclusion that they, at all events, did the least harm.

The treatment through the ear by means of cotton plugs saturated with camphor should have a passing mention. Hüppe, in experiments on dogs and horses, found that he could produce deep narcosis by pouring 10 to 30 gm. of sulphuric ether into the ear, and any one who has seen the benefit that quickly results from this method of administration of medicine in toothache cannot consider the trial of this simple and harmless method in whooping-cough as frivolous, though absolute results are not to be expected.

After so many commendations of different remedies and different methods, we can only conclude that every physician is handiest with his own tools, and for those whose work has been met with contradiction we offer the words of Friedrich Hoffmann: "If you wish to understand my arcana, then learn my methods."

In reference to the treatment of complications, Desruelles' warning is still serviceable: "Presque toujours plus graves que la coqueluche, les complications doivent être énergiquement combattues, comme si la coqueluche n'existait pas. Elles deviennent les maladies principales, et le danger, qu'elles présentent, doit constamment régler la conduite du praticien."

It is not necessary to discuss very fully here the treatment of the febrile bronchitis or the catarrhal or croupous pneumonia of whooping-cough. The duty of every practitioner is to throw aside the narcotics and give at once tartar emetic on hearing the faintest crepitant râles in the lungs. Asthmatic attacks in whooping-cough are peculiarly benefited by small doses of potassium iodid and niter paper. Potassium iodid (0.03 to 0.1 daily to children of from one to five years) is naturally

contraindicated in fever with intense irritability of the larynx and any inclination to hemorrhages. In two cases of spasm of the larynx and rapid repetition of the paroxysms, Taub intubated successfully, thereby "saving life."

In simple congestion of the brain the neutral salts and mineral acids, especially the elixir acidum of Haller, do good service. Symptoms of more intense irritation with delirium do good under an enema of valerian infusion (spec. valerian., 5.0 : 100.0) or an emulsion of asafetida (0.2 to 0.5 : 100.0). The first symptom of inflammation of the brain should be met by purgative doses of calomel.

Disturbances caused by the violence of the cough are avoidable in so far as the cough is amenable to treatment. Hemorrhages usually cease of their own accord, though from the nose they are sometimes obstinate, but even then they commonly yield to injections of fresh lemon juice (a teaspoonful at a time) or cotton tampons saturated with turpentine. Bleeding from the nose in a hemophilic, requires the internal administration of mineral acids, liquor ferri perchloridi, and similar empiric remedies.

Preventive measures against injuring a hernia, as by bandaging, are seldom successful. The best results are obtained from the application of a belly-band and instruction to the patient to flex somewhat his thighs on his abdomen during a paroxysm.

The surest ally, best nurse, and most careful warden for the little patient is a vigilant, solicitous, intelligent mother. Without her, the cleverest physician spends his time in vain.

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BOSTOCK'S SUMMER CATARRH.

BY

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BOSTOCK'S SUMMER CATARRH.
(SO-CALLED HAY-FEVER.)

HISTORY AND GENERAL DESCRIPTION.

AT the beginning of the last century, John Bostock, a celebrated physician, chemist, and physiologist of London, related, on March 16, 1819, before the Medical and Chirurgical Society of that place, in the following words, the history of his own case as an example of an uncommon symptom-complex, under the title of a "*Case of a Periodical Affection of the Eyes and Chest*":

"J. B., aet. forty-six, is of a spare and rather delicate habit, but capable of considerable exertion, and has no hereditary or constitutional affection, except various stomach complaints, probably connected with or depending upon a tendency to gout. About the beginning or middle of June in every year the following symptoms make their appearance, with a greater or less degree of violence. A sensation of heat and fulness is experienced in the eyes, first along the edges of the lids, and especially in the inner angles, but after some time over the whole of the ball. At the commencement, the external appearance of the eye is little affected, except that there is a slight degree of redness and a discharge of tears. This state gradually increases until the sensation becomes converted into what may be characterized as a combination of the most acute itching and smarting, accompanied with a feeling of small points striking upon or darting into the ball, at the same time that the eyes become extremely inflamed, and discharge very copiously a thick mucous fluid. This state of the eyes comes on in paroxysms, at uncertain intervals, from about the second week in June to the middle of July. The eyes are seldom quite well for the whole of this period, but the violent paroxysms never occur more than two or three times daily, lasting an hour or two each time; but with respect to their frequency and duration, there is the greatest uncertainty. Generally, but not always, their invasion may be distinctly traced to some exciting cause, of which the most certain is a close moist heat, also a bright glare of light, dust or other substances touching the eyes, and any circumstance which increases the temperature. After the violent inflammation and discharge have continued for some time, the pain and redness gradually go off, but a degree of stiffness generally remains during the day.

"After this state of the eyes has subsisted for a week or ten days, a

general fulness is experienced in the head, and particularly about the fore part; to this succeeds irritation of the nose, producing sneezing, which occurs in fits of extreme violence, coming on at uncertain intervals. To the sneezings are added a further sensation of tightness of the chest, and a difficulty in breathing, with a general irritation of the fauces and trachea. There is no absolute pain in any part of the chest, but a feeling of want of room to receive the air necessary for respiration, a huskiness of the voice, and an incapacity for speaking aloud for any time without inconvenience. To these local symptoms are at length added a degree of general indisposition, a great degree of languor, an incapacity for muscular exertion, loss of appetite, emaciation, restless nights, often attended with profuse perspirations; the extremities, however, being generally cold. The pulse is permanently quickened from 80, the average standard, to about 100, and upon any considerable exertion it rises to 120 or more.

"This is an account of the complaint in its worst state, which, however, it does not assume in every season; and, indeed, its violence is generally less than is here described. The affection of the eyes is recollected to have occurred when the patient was eight years old, and there has been more or less of it every year since; the sneezings came on nearly at the same period, but the first attack at the chest was at the age of sixteen or seventeen. Generally speaking, the complaints have increased for the last twenty years, although not progressively. All the acute symptoms disappear about the end of July, but a considerable degree of weakness and languor is left, which remains a month or six weeks longer. It has happened that the most severe summer complaints have been experienced after the patient had enjoyed the best health during the preceding spring. On the contrary, it has been thought that after a severe summer attack, the patient has more completely and more rapidly regained his usual state of health and strength in the autumn.

"The remedies employed have been various, and they have been persevered in with an unusual degree of steadiness. Topical bleeding, purging, blisters, spare diet, bark and various other tonics, steel, opium, alterative courses of mercury, cold bathing, digitalis, and a number of topical applications to the eyes, have been very fully tried, but it is doubtful whether any distinct or permanent benefit has been derived from any of them. The complaint once seemed to be decidedly stopped by a journey, but in other instances it has existed while the patient was traveling. By using every means for obtaining fresh air, without much exertion, and by carefully avoiding a moist and close atmosphere, the symptoms may in some measure be kept off, but they have frequently appeared under circumstances that seemed the least likely to have produced them.

"It may form an important addition to the narrative to state that during the last summer the patient was so situated as to be able to avoid almost every degree of bodily exertion; he remained nearly confined to the house for about six weeks, and the result was that, notwithstanding the unusual warmth of the season, he experienced much less of the affection than he had done for several years before."

This graphic picture of the affection, containing in a nutshell almost all that can be said about the disease to-day, was entirely unknown to the medical writers before Bostock.

Heberden (1801) alone may have seen it several decades earlier than his London colleague: "I have known it (scil. catarrh) return in four or five persons annually in the months of April, May, June, or July, and last a month with great violence." Yet how little he thought of a special disease is evident from his Latin commentaries in Friedländer's works: "Quinque ægris contigit graviter laborare hoc morbo (scil. destillatione) per mensem omni æstate."

Neither Bostock himself, who in 1828, nine years after his first communication, gave another fuller and more detailed description of *catarrhus æstivus*, or *summer catarrh*, based on a study of 28 new cases, and in which he pointed out Heberden's remarks, had found in the older literature examples of his malady; nor has Philipp Phöbus, the author of the most celebrated monograph on Bostock's catarrh, or August Hirsch, the well-known investigator of historic pathology, discovered any intimation of the disease in the writings of the earlier physicians. And after rooting through more than two hundred ancient books and treatises on catarrhus and destillatio, sternutatio and asthma, on periodic and intermittent diseases, I must confess that my efforts to find a rival of Bostock's have been likewise in vain.

Others, John Mackenzie, for instance, have been more fortunate, yet only because they ignored Bostock's clean-cut description and called every spasmodic sneeze and asthma, hay-fever. Consequently, they found it easy to point out the disease in Galen, and demonstrate as a common occurrence an affection which, up to the time of Phöbus, and even in our day among the majority of physicians, is reckoned infrequent.

It is necessary to keep the actual picture well in mind in order to judge whether it is a newly described disease or a form of the earlier known catarrhal diseases, especially coryza nervosa, or asthma convulsivum.

All cases observed by Bostock and collected by careful writers seem to have these symptoms in common: *Annually, in certain individuals, there appear in regular order secretory and convulsive disturbances produced by irritation, in the eye, then in the nose, later in the deeper air-passages, with daily exacerbations and remissions. This is accompanied by an uncommon sensitiveness to certain external irritants, and winds up in a catarrhal inflammation of the different mucous membranes. All these symptoms develop gradually, in the course of a certain number of weeks, they remain stationary for about a week, and then gradually disappear, leaving a condition of perfect health. The typical course which each case takes in the individual year also declares itself in the whole category of cases according to the time of life of the patients. For instance, in*

childhood it is only the eyes and nose that are affected, in adolescence a certain amount of asthma is added, and in manhood this becomes a prominent symptom.

The conjecture seems natural that this picture is sufficiently typical to prevent confusion with other diseases of the same organs.

The first writers to confirm Bostock's description were MacCulloch in London (1828), Gordon in Edinburgh (1829), and Elliotson in London (1831). They agreed entirely with Bostock's description, though they differed in their opinion as to the causal origin. While Bostock rejected the popular designation that came into use between the time of his first and second communications, the others maintained that the name *hay-fever*, or *hay-asthma*, which " had lately become fashionable " (MacCulloch), was the proper designation for the new disease.

It is unintelligible how the name *hay-fever* was all of a sudden so widespread in Southern England in 1828 that Bostock assumed it as well known. The opinion that the aroma from hay was the cause of the disease must have arisen between 1819 and 1824, for Elliotson, in his paper, announces that he first heard it in 1822 or 1823, and it was entirely unknown before Bostock's original communication. Phöbus surmises, and probably with reason, that the sudden rise and notoriety of the name were due to some unknown semipopular writing.

The cause attributed to hay-fever quickly took on a specific form. It was sought by Gordon in the sweet-scented vernal grass, and Elliotson also blamed the aroma of the Anthoxanthum odoratum; not, however, that of the dried grass, but that of the fresh grass, when in flower, and not its scent, as some of the patients did, but " probably the pollen."

Ignorant of the writings of the English physicians, therefore independently of the first discoverer, Cazenave, a physician of Bordeaux, described in 1837 a case of summer catarrh, with its proper symptoms, under the title: " Eternumens, et coryza annuels suivis de la phlegmasie successive de plusieurs membranes muqueuses."

Not long afterward, however, the old yet daily renewed experience in nosology was verified—namely, that no sooner does any one evolve a clear and simple picture of disease from the complicated mass of symptoms, than blear-eyed stupidity is sure to come along to blur the features of the picture or confuse with it closely similar or sometimes totally dissimilar pictures.

In this way Wilkinson King, in 1843, was able to deny any peculiarity to Bostock's disease, which he had never observed, by neglecting the criterion of its annual return at a definite time, and confusing summer

asthma with other common catarrhs and asthmas. John Hastings did the same in 1850. Fortunately, there were other physicians who had the opportunity of studying catarrhus æstivus in themselves and their clients, and from them we have a series of faithful observations, which, for the time being, rescued the disease. Among these may be mentioned the English physicians Gream (1850) and Kirkmann (1852) and the French physician Fleury (1859), who described the picture in themselves, and F. William Mackenzie in London (1851), and Cornaz in Neufchatel (1860), who made their observations on others. Fleury called it "maladie de foin"; Cornaz, "catarrhe des foins."

The first in Germany to give an accurate account of the disease, more accurate than any one before, and perhaps after him, was the Professor of Medicine and Pharmacology at Giessen, Phöbus. He obtained his material from a careful study of existing publications, from the answers to questions contained in a circular, addressed to physicians, medical societies, and scientific bodies generally, and also to the medical journals. Apart from personal experience with the disease and Bostock's classic description, this work will always remain the most important source of knowledge on the subject. Its only error is perhaps a too pedantic thoroughness. His pains to estimate the exact nosologic limits and elements of a "*Typischer Früh-sommer-katarrh,*" so-called hay-fever, Heuschnupfens, rye-asthma, to define the entire connection of its individual symptoms compared with other forms of catarrh, isolated irregular cases of a nervous "cold," of a habitual asthma paroxysm, seem to have been in vain, especially for the majority of later physicians, who, through ignorance, either deny the existence of Bostock's catarrh as an independent affection, or discover it where it does not exist. Phöbus himself said: "The disease has comparatively often endured the experience of being seen where it was not, and not being seen where it was"; moreover, "among many, especially women, it has come to be the proper thing to call every catarrh hay-fever."

The fact that many patients suffering from Bostock's catarrh are, at the time of their affliction, extremely susceptible to the emanations from certain plants and parts of plants, and that therefore the disease has been attributed to these as its cause, is remembered by but a few. From this many jump to the conclusion that every attack in which any probability of a suspicion could be thrown on these plants was to be included under hay-fever. Moreover, when the hypotheses of Elliotson (1831), and Gream (1850), that the causa nocens was associated with hay, grass, flowers, and pollen, were confirmed and seemingly proved by the experiments of Elliotson, Simpson (quoted by

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Phöbus), and especially Blackley, then *pollen-catarrh*, hay-fever, and
Bostock's catarrh became at once identical.

Herbert relates the following: "A kinswoman was accustomed to
accompany her children to a corn-loft, where they played. But in a
short time she found herself obliged to discontinue her visits, because
every time she was attacked by an intense filling up of the head. Avoid-
ing this custom, the catarrh did not return."

This case is in no way different from Trousseau's personal experience:
"My suspicions became aroused in relation to the faithfulness of my
coachman. In order to convince myself, I climbed to the granary and had
him measure the oats in my presence. During this operation, I was
seized with such a dreadful oppression that I was scarcely able to make
my way back to my room. My eyes stood out of their sockets, and on my
pale, swollen countenance lay an expression of unspeakable anxiety. I
am not a smoker, yet on this occasion I lit a cigar and took a few whiffs.
After eight to ten minutes the attack terminated. What could have
caused it? Evidently, the shaken-up dust of the oats aspirated into my
bronchi. Hundreds of times I have walked the streets and boulevards of
Paris in an atmosphere of much thicker dust, yet I never experienced any-
thing similar. Therefore, the cause in this case must have been some-
thing peculiar. Moreover, it surprised me in quite exceptional circum-
stances. Under the influence of the mental excitement brought about by
the idea of a domestic theft, my nervous system was strongly affected, and
an ordinarily slight cause was sufficient to produce a marked impression."

There is no reason why both these cases and many similar ones should
not be designated hay-asthma, as is done by Herbert, but not by Trous-
seau. Yet it is unnecessary to employ the same designation for Bostock's
catarrh, with which these descriptions have nothing in common except the
sensitiveness to hay-dust.

Abbott Smith reports the history of Dr. Rowe, who suffered from true
summer catarrh. In the course of it we read the following: "For some
years I remained at home on account of my asthma attacks. When I was
almost well, I received a visit from two friends, who doubted my word as
to the origin of my disease. Therefore, one of them brought with him a
bouquet of flowers and shook it about the room before I appeared, in order
to distribute the pollen in the air. As I entered the room I began to
sneeze violently, and was seized by an asthma paroxysm that lasted fif-
teen hours."

The difference between this and the previous case is that the first
two patients were sensitive to the smell of hay, without a yearly recur-
ring summer catarrh; while the last was sensitive only during his
annual catarrh. Trousseau and Herbert give examples of the old
orthopnœa ab antipathia, of idiosyncratic sneezing and asthma, the
attacks of which occur regularly under the influence of special causes,
peculiar to the individual; while Rowe suffered from Bostock's
catarrh, which makes the person susceptible at a definite season to
otherwise harmless influences, and this antipathy or idiosyncrasy re-
mains only as long as the critical period lasts.

If the common name hay-fever or hay-asthma is to be conferred on these cases and a hundred others externally similar, we have no objection; yet we shall then speak also of violet-cold, and camphor-cold, of pollen-asthma, ipecac-asthma, featherbed-asthma, etc., naturally with attention to the clinical histories which Beau, Trousseau (vol. II, Lecture 52, " On Asthma"), and others have preserved.

Rose-catarrh, rose-asthma, and rose-fever are also spoken of as special diseases. Dunglison (1860) reports on rose-catarrh in North America; Simpson (1866), quoted by Phöbus, on rose-fever in the United States; Maddock (1865) finds in England rose-cold; Morill Wyman in 1872 devotes a monograph to it; and Morell Mackenzie and Ziem (1865) described rose-cold and Rosenschnupfen as " a variety of hay-fever."

If the histories are now carefully studied (supposing such to be given) in relation to the separation of "rose-cold" as a special disease, it is quickly discovered that the same cases are to be differentiated as in "hay-fever." One has his annual summer catarrh, during the course of which he is sensitive to the aroma of roses, while at other times he may handle these with impunity; the other is attacked by his coryza, sneezing paroxysm, asthma, vertigo, or whatever it may be, always at the sight of a rose, no matter where or when it appears, or even by the odor. The clinical history of the latter class ordinarily reads somewhat thus: A lady or a gentleman of middle age—and, remarkable to say, the latter is almost always a canon or a cardinal—is attacked by a short or continuous severe coryza or something similar every time he smells a rose, and is thereby forced to go out of his way to avoid these flowers, to banish them from his room and garden, or to live in continual dread of them.

After a few writers had succeeded, to their own surprise, in exhuming such observations from the old and even most ancient literature, they drew for themselves the following conclusions: "Bostock's catarrh occurred even in Galen's time, for there were then persons with an idiosyncrasy to roses; but whether this sensitiveness is toward roses, or hay, or pollen, makes no particular difference; therefore, we deny the peculiarity of Bostock's disease." Since, now, it was further discovered that almost all imaginable perfumes had called forth in this or that individual an "idiosyncratic catarrh," "nervous asthma," etc., Bostock's catarrh, in which all these idiosyncrasies have been noted, must be nothing else than an accumulated result of these.

With tiresome monotony since Biermer's excellent work the following passage from van Helmont (1644) has been quoted in fifty and more

papers on hay-fever: "Vidi frequenter mulieres, quæ suavi olentium odore præter cephalalgias et syncopes confestim in extremam respirandi difficultatem inciderent." If van Helmont had been read a little more carefully, more examples would have been discovered in his work, but at the same time it would have come to light that these passages referred expressly to examples of hysteria; but every one was too happy in the discovery of a proof that Bostock's disease was known in the seventeenth century.

The fact was overlooked that Phöbus had collected a series of much more convincing observations from the literature of the seventeenth and eighteenth centuries, in order to show that they did not correspond to a typical Bostock's catarrh (Joh. Rhodius, 1657; C. v. Schneiderus, 1662; Robert Boyle, 1691; Vitus Riedlinus, 1695; Triller, 1766). These may be read in Phöbus, or, better, in the originals, and if any one is interested in a whole collection of similar observations in the sixteenth and fifteenth centuries, I would refer him to the "Observationes rariores" of Joannes Schenkius, or Leonardo Botallo, or Joannes Echtius.

I will, however, quote a few observations from other old books in order to compare them with recent notices: Ziem (1884) relates the case of a man whose eyes became inflamed at every rose season, and Münich (1892) one of an acute rhinitis every time tomatoes were eaten; three hundred years before, Marcellus Donatus (1586) reported the case of a boy whose lips became swollen and his face covered with red and black specks every time he ate eggs. When Morell Mackenzie (1883), in order to prove that hay-fever was due to an idiosyncrasy of the nose, recalls Schiller's partiality for rotten apples, without which the poet could neither live nor work (Lewes, "Life of Goethe"), it may be worth while to mention that four hundred years before Schiller, the King of Poland, Jagello, according to Martinus Cromerus, had such a distaste for apples that he fled from their aroma as if it were the most fatal poison. Wyman (1872) recounts cases where the emanations of all kinds of animals—cows, dogs, cats—produced "hay-fever" symptoms, and Hack (1886) one of a sensitive English woman who was not affected by pollen during hay-fever time, but manifested the most severe dyspneic attacks if a cat approached her, and a cotton tampon in the nose was her only protection against it. Two hundred years earlier, according to Riedlin, the Duke de Schomberg (1693), "with many Germans of that day" ("mit vielen damaligen Deutschen"), reported that he could not bear not only the sight of a cat, but even the odor of a hidden one, without dyspnea and vertigo, and others of his time were similarly affected by the smell of mice and dogs. I know a good-natured man whom the aroma of a burning cigar arouses to violence and in whom it causes a swelling of the conjunctival and nasal mucous membrane lasting some hours. Even the thought that some one might bring a cigar into his house is frequently sufficient to produce burning of the eyes and dryness of the nose. But as far back as 1563, Lusitanus reported cases that suffered from the smell or eating of cheese, the same as if it were poison. Many in our day experience asthmatic attacks from going through a tunnel; but what is this compared with the individuals mentioned by Paraeus, the celebrated surgeon (1590), and Weinrichius (a name unknown to me, but quoted by Schenck), who fell into a faint at the sight or smell of an eel? One even was affected by the most terrifying anxiety if an eel was concealed in the house. Down (1862) relates a case where the picture of a harvesting was sufficient to induce "hay-fever" in an Irish woman, and

John N. Mackenzie one of a very nervous woman, affected for years with "attacks similar to hay-fever," who went into a paroxysm when an artificial rose was brought near her. He might also have related that a Venetian, a friend of Amatus Lusitanus (1563), suffered likewise from attacks at the mere sight of a rose.

I am afraid these "antiquities" may prove tiresome to the reader, yet I wished by a superfluity to surfeit the writers who seem to be ignorant of all but modern curiosities, and to subvert the opinion that anything is poison, by these ancient and well-known stories, either for or against Bostock's summer catarrh or hay-fever taken in Gordon's sense.

The confusion in regard to hay-fever was not yet at its height when writers began to speak of "rose-fever," and "stable-fever," and "concert-fever," and "railroad-fever," of "sun-fever" and "dust-fever" (George Beard), and of "peach-cold," as equally authoritative forms of "rhinitis vasomotoria periodica," as J. N. Mackenzie designated Beau's old "*asthmes de cause accidentelle.*"

The story became complete when Daly (1882), of Pittsburg, and Hack (1883), of Freiburg, proved the connection between anatomic or functional changes in the nasal mucous membrane and a series of nervous colds, asthmatic attacks, etc. At once Bostock's catarrh, vulgarly hay-fever, became a reflex disease which, like every periodic paroxysm of sneezing or nasal discharge, or asthma attack, must have its anatomic seat and origin in the nose. Now every rhinologist, especially in America, observes annually dozens of hay-fever patients, treats them, and—cures them.

"Puisque c'est dans les fosses nasales que se trouve le point de départ du mal, c'est là qu'il faut faire porter l'effort thérapeutique. Ce malheureux tissu caverneux ou érectile, encore discuté, ces lésions variables parfois bien peu évidentes, on les a poursuivis par le fer et le feu . . . on a brûlé d'une façon impitoyable . . . on a même enlevé les cornets. Des chiffres d'opérations effrayants ont été publiés en Allemagne et surtout en Amérique" (Leflaive).

Every unprejudiced mind sees the confusion brought about by superficial observers, when they designate every convulsive cough as whooping-cough, even though its tone only recalls the "crow" of that disease; the same confusion exists between Bostock's catarrh and every possible paroxysm of sneezing or dyspnea, because there happens to be a striking symptom of the former. Moreover, the theory of many physicians, that because most external irritations will produce a paroxysm in whooping-cough, therefore the disease is nothing more than an irritative cough, due to a lesion in the larynx, is about as logi-

cal as the conclusion of the majority of modern writers on "hay-fever," who say: Because certain irritations excite or augment an asthmatic attack in Bostock's catarrh, therefore every asthma that is produced by these irritations is identical with Bostock's; and vice versâ. The trouble is they usually formulate their theory before they know the disease symptoms. We intentionally repeat: The individual suffering from Bostock's catarrhus æstivus, from catarrhe d'été (Laforgue, 1859), from catarrhe d'été sans fièvre de foin (Hervier, 1861), from hay-fever in its original signification, shows frequently, even in childhood, an inclination to be attacked every year in early summer by a catarrh of the eyes and air-passages of several weeks' duration. This produces marked secretory symptoms of irritation, and affects in order the eyes, nose, throat, and chest. It causes extraordinary sensitiveness on the part of the patient to direct or indirect external irritations, and gradually, step by step with the diminution of this increased irritability, terminates in complete health, till the next year brings a new attack. The inclination to the disease exists through life. During youth it is commonly limited to the eyes and nose, but with increasing years it extends deeper and deeper into the chest, so that during early life inflammation of the eyes and coryza predominate; during later life, asthma. The outbreak of the affection, and the aggravation of its symptoms, depend on certain external influences, different in different patients, and effective only at a particular season of the year, so that outside the critical period the patient may expose himself with impunity.

COURSE AND SYMPTOMATOLOGY OF HAY-FEVER.

From many statements in the literature there can be no question that, besides the outspoken form of Bostock's catarrh, there are *abortive forms*. In our sketch we have kept to the typical disease, for any one who understands this perfectly can easily differentiate the "formes frustes." Moreover, it is not advisable to describe the abortive forms of a disease the type of which is so little recognized that within the last ten years its very existence has been frequently denied, its nature more frequently misunderstood, and itself, with unprecedented obstinacy, robbed of its name in favor of other diseases.

Yet, taken altogether, Bostock's summer catarrh runs its course with a uniformity that is almost monotonous, and its symptomatology shows not so marked deviations in its individual elements as we see in many another disease.

Absolute similarity in the attacks seems to be extremely rare. Cornaz relates the case of a female patient in whom the disease began at the age of nineteen, and at the age of twenty-three the attacks "remplacé par une urticaire, qui dura aussi de six à sept semaines." And a Dr. Kirkman wrote to Phöbus that before his first attack of hay-fever, he had a nettle-rash every June. This never recurred after the advent of the former. In discussing the etiology of the affection, we will return to the relation between Bostock's catarrh and urticaria.

As to the *influence of other diseases complicating* Bostock's catarrh, I have found nothing. Guéneau de Mussy and Leflaive report that pregnancy aggravates it.

We have already mentioned the fact that the disease frequently begins in childhood. Phöbus reported the earliest authentic beginning at five and one-fourth years. Morell Mackenzie saw first attacks in one child of two years, and in another three years old. Both little ones were children of parents who themselves suffered from the disease, otherwise it would have been overlooked or not recognized. According to Phöbus' statistics, the disease in 56 patients manifested itself first 10 times in the second quinquennium, 7 in the third, 11 in the fourth, 9 in the fifth, 5 in the sixth, 7 in the seventh, 6 in the eighth. After the "juventus" of the Romans, or, in other words, the fortieth year, the disease seems to arise only exceptionally. Wyman's statistics are quite different. According to them, of 72 cases, 11 arose in

the first decennium, 15 in the second, 25 in the third, 8 in the fourth, 11 in the fifth, and 2 as late as the sixth.

George M. Beard's statistics differ altogether from both. This observer meanwhile mars the conception of Bostock's catarrh. Of 188 cases, the disease began in 34 during the third decennium, 56 during the fourth, 65 during the fifth, and 53 during the sixth.

Some patients are able to give the day and hour when the first attack took place, as at a harvesting, a country picnic, etc.

The first attack, or even the first three to six attacks, are often mild, and sometimes are unrecognized by the inexperienced. As already mentioned, the picture becomes more characteristic in the course of years, inasmuch as in youth only the eyes and nose are affected, while later the throat and chest participate, so that finally the purely catarrhal symptoms pass over into the asthmatic. General disturbances, like prostration, weakness, and fever, seem to depend not so much on ages as on the individual constitution. Many patients' experience a gradual decrease in all symptoms with the setting-in of old age, though traces of the disease remain for life. Some cases show a continuance of severe attacks for fifty or more years; and when cure is spoken of, it usually only means marked improvement in the symptoms, or, at most, the omission of an annual attack Complete recovery is decidedly questionable.

In relation to a celebrated case, that of the physicist Helmholtz, I know from Binz that for a number of years he experienced amelioration, but not cure, of the symptoms by the use of quinin, which Helmholtz himself recommended for this disease. In spite of many endeavors to learn more of the ultimate course of the malady in this patient, I have never been able to learn anything certain.

The statements of many specialists, especially in America, as to almost numberless cases of cure, contradict so decidedly general experience that it is not unreasonable to say that most of the patients were not affected with Bostock's catarrh, true hay-fever; or that, tired of the energetic treatment, they finally remained away. Moreover, the continuance of the United States Hay-fever Association proves only too well how little confidence those afflicted with the disease have in the results obtained by their physicians.

Among all the symptoms of Bostock's catarrh, asthma is, unquestionably, least inclined to improve in later years.

How long life is compatible with the disease is shown by the many reports of it in decrepit old people.

Morell Mackenzie relates the case of an old man, almost ninety years of age, who was attacked every year regularly till his death. Phöbus reports the only case in which death might be attributed to the attack:

A man of fifty-nine years, in whom the ordinary annual attack had progressed a few days, died suddenly with symptoms of a very acute suffocative catarrh. The postmortem revealed edema of the lungs and a hyperemia of the brain with some fluid blood in the ventricles.

The *omission of separate annual attacks* is under special circumstances possible. Patients who in Europe suffer yearly, may not be affected while at the Cape or in India (Salter Rowe, Phöbus). Patients living in the towns or lowlands of North America frequently protect themselves by their timely removal to an elevated immune site (Break, Beard, and others). Others are benefited by a sea voyage or strict seclusion indoors. That all these measures may prove futile has been shown by Simpson, Walshe, and others; that they are at most protective only for that year, almost all agree.

Between the summer attacks, some patients, as has been mentioned, show mild relapses in the late summer or autumn. This observation was first made by Elliotson; later, other relapses were reported by Travers, Leforgue, Phöbus, and others. Parriot, Guéneau de Mussy, Leflaive, and others, record the second attack as taking place in August, September, or October. According to Morill Wyman, Beard, and numerous confirmatory observations by others, in North America the spring attack is usually milder than the autumn one, and they are differentiated by the name June- or rose-cold, and autumnal catarrh. Hack reports an exclusively autumn catarrh in a German; Emond, in an Englishman.

The date on which the annual attack begins is subject to no slight variations according to the individual, the country, and the climate. In England, Belgium, France, and Germany, the beginning of the attack is, as a rule, in the second half of May or the first days of June; but in North America August is the period during which the typical hay-cold, hay-catarrh, or hay-asthma begins; while during June, rose-cold runs its course.

Phöbus reports a typical spring catarrh in a teacher aged fifty-one, which began annually since his twenty-ninth year at the end of March or commencement of April. Hack reports an autumn catarrh in a professor, aged thirty-four, which began regularly for twenty-two years in the second half of August.

A variation in the time of the attacks in individual patients, so that the critical period changes from spring to summer or autumn, has not been observed.

It is obvious from the foregoing that when Decaisne denies a regular periodicity to the disease, he has either seen no case of it, or misunderstood

its symptoms. The same is true of the irregular attacks reported by Pirrie, Moore, and Waters. It is generally conceded that in the same patient the commencement of the yearly attack may vary a couple of days, and Cornaz' day-book in reference to a patient well illustrates this. In this case the attacks began in:

1830 on May 15.	1854 on May 20.
1848 " " 22.	1855 " June 6.
1949 " " 23.	1856 " " 1.
1850 " " 28.	1857 " " 5.
1851 " " 17.	1858 " May 28.
1852 " " (end of).	1859 " June 1–5.
1853 " June 2.	1860 " May 24.

The variation, therefore, in this case extended over twenty-two days, from May 15th to June 6th.

In different places the patient may find the beginning of the attack anticipated or postponed beyond ordinarily normal variations.

English patients, for instance, state that while sojourning in southern countries, their attacks appeared earlier than usual. An English physician, Dr. Woomann, asserts this of himself while he lived in the tropics, Egypt, Bombay, China, at the Cape, and in Madeira, whence he returned occasionally to England. A correspondent of Phöbus reported that in southern England, in the neighborhood of London, his attacks began in the last week of May or first week of June; in Switzerland, in the middle of May; and in Yorkshire, not till the 10th to the 20th of June.

The *duration* of the annual attacks is much the same in all cases, being usually from six to eight weeks, though it may last only a month or continue for three months. This is true, not only of our early summer catarrh, but likewise for the North American autumn catarrh. According to George Hayward, the June catarrh, or rose-cold, seen in the United States, runs a shorter course, usually from about three to four weeks.

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The *annual attack* is ordinarily ushered in with distinct premonitory symptoms, which usually last about two or three days, or sometimes only a few hours, though they may be entirely wanting. This *prodromal stage* is absolutely denied by the followers of the pollen theory; nor is it at all consistent with this hypothesis, which we will discuss later.

Frontal headache and general malaise are complained of by one; digestive disturbances, unwonted heaviness and somnolency after eating, and ill humor, by another; disagreeable local sensations in the eyes or nose, by a third. Guéneau de Mussy reports an edema of the

face in one case, irregularity in menstruation during the months of March and April in another, as premonitory symptoms.

The occurrence of local symptoms, and with them the commencement of the *principal stage*, is usually sudden. In cases where premonitory symptoms fail, this stage frequently breaks out as the consequence of some cause. For instance, in a female patient mentioned by Phöbus, it originated two years in succession immediately on the reception of a bouquet of grasses and wild-flowers.

The attack develops usually in the following way: The patient notices first at the inner angle of the eyelid a slight itching, tickling, or burning, which becomes more intense, and in a few minutes extends over the margins of the lids and the entire conjunctiva, producing intolerable smarting. This is soon associated with an irritation or stinging in the nose, leading to almost endless sneezing. This irritation ascends to the frontal sinuses, and finally settles, not rarely as an intense itching, on the tip of the nose, accompanied by a profuse flow of tears and marked photophobia. The sneezing continues so violently and irresistibly that the patient can scarcely "catch" his breath between the sneezes.

This sneezing begins with a sudden deep inspiration, followed, after a short interval, by a noisy, forcible, short expiration. The patient stands a moment motionless, without drawing breath, for he feels that the second forcible explosion is about to take place, following which is a third, fourth, etc. At the height of the disease he sneezes ten, twenty, thirty, even sixty times in succession, often without time or courage to draw between the sneezes a few hasty breaths. Entirely absorbed in his paroxysm, he exerts every effort to suppress the sneezing, and is successful only when, covered with sweat, he is on the verge of exhaustion. The paroxysms often leave behind intense pain in every muscle of his thorax. The least motion, the slightest draft of air, produces a repetition of the attack; even the movement of the hairs (vibrissæ) at the entrance to the nose may be sufficient, so that they are sometimes cut off by individual patients. Yet under conditions of the greatest tranquillity the paroxysm is repeated several times daily, especially during the forenoon, and it sometimes takes place even at night. During any single day the attacks may be repeated so often that, as related by Fleury, the sneezes may be counted by many hundreds. Sudden outbreak, absolute irresistibility to the irritation, intense forcibleness of the explosion, and frequent repetition are the characteristics of the convulsion.

There is, besides, an unparalleled discharge from the nose, often so

profuse as to soil dozens of handkerchiefs in a day. This terminates with a considerable swelling of the nose.

After hours, days, or weeks the irritation of the mucous membrane extends into the throat, and over the palate, beginning with dryness and burning, and leading frequently to profuse secretion. At the same time the patient sometimes complains of stinging in the nose.

A dull or sharp headache is always felt at the commencement of the attack, and increases hour by hour. During the attack it may manifest itself as intense shooting pains in the forehead.

On a careful examination of the affected organs during the first minutes or hours of the attack, the mucous membrane is usually normal, or, at most, in a condition of hyperemia. The profuse discharge from the conjunctiva and nose is clear, watery, and poor in solid constituents. That from the nose is usually alkaline, and so pungent as to cause swelling, redness, and chafing of the alæ of the nose and the upper lip.

Only after the continuance of the symptoms, under the influence of the copious secretion, and especially the attempts of the patient to still the unbearable itching with rubbing, does the hyperemia of the mucous membrane pass over into painful inflammatory swelling. This may lead, in the eyes, to chemosis and edema of the lids, even to a bleb-like bulging of the thick, swollen conjunctiva; in the nose, to complete obstruction, necessitating mouth breathing; in the throat, to tormenting swallowing movements and painful deglutition.

The hyperemia of the conjunctiva is limited to the caruncle or extends to the cornea. It produces a sensation of stiffness in the eyelids, of tension and fulness in the eyeball; while the flow of tears, which is frequently accompanied by a visible swelling of the lacrimal glands, remains profuse, the secretion from the conjunctiva is slight. But with the remission of the former, there appears a thick mucous discharge, accompanied sometimes by an increase of secretion from the Meibomian glands. The follicles may then show considerable swelling.

The sneezing and discharge of tears affect each other in a vicious circle, in that, by the former, the lacrimal glands are irritated, and by the flow of tears through the nose, a new irritant is continually being brought in contact with the nasal mucous membrane. Excoriation of the cheeks by the flowing tears is at all events rare.

As a rule, both eyes suffer similarly and simultaneously; yet one eye may be affected earlier or more severely than the other, and alterations in the severity of the symptoms in both eyes have been reported.

Like the conjunctiva, the nasal mucous membrane exhibits after the appearance of the nervous irritative symptoms the signs of inflammation, or rhinitis. The secretion, which up to this time was transparent and watery, becomes thick and opaque. The nose, previously pale and cold,—Roberts asserts the marked coldness of the tip of the nose during an attack as the "pathognomonic sign of hay-fever,"—now becomes, especially at its base, red and swollen. Epistaxis is seen in individuals under twenty years of age occasionally; later, only exceptionally.

Yet, even when the copious secretion is at its height, there may be no apparent change in the nasal mucous membrane. And, again, it may happen that at the very commencement of the attack the nose is occluded by swelling and congestion, yet dry, and beginning to secrete only after two, three,—twenty-four hours.

After a number of days or weeks the profuse secretion diminishes, and becomes, even during the paroxysm, thick and turbid.

It is noticeable that the sense of smell practically never suffers during or after an attack. In regard to this, Cornaz reports a patient who remarked this difference between an ordinary cold, which he sometimes had in the winter, and his hay-fever in spring, that he usually lost his sense of smell with the former, but never with the latter. A woman of fifty recounts that she not only experienced no decrease in the sense of smell during an attack, but such an increase in acuteness that a bouquet of flowers in a room far removed from her became troublesome on account of its scent. As in the eyes and in the nose, so there arise in the throat, after a transitory sensation of dryness, paresthesiæ of tickling, itching, smarting, and burning. They are felt in the vault of the pharynx from the Eustachian tubes to the posterior nares, over the soft palate, and on the tongue, and may become so intense as to be compared by the patient to the eating of cayenne pepper. For the purpose of lessening the burning, the patients press the back of the tongue against the palate or rub the tip of the tongue on the gums, make rapid swallowing movements, or bury the ends of their fingers in their ears.

Locally, we see active hyperemia and moderate swelling of the throat and palate; later, a profuse secretion of mucus. The ring of lymphoid tissue around the pharynx remains unaffected, though the submaxillary glands are swollen.

Some complain of an itching sensation on the face, especially over the irritated cavities. Salter reports it on the chin and under the chin as an early symptom of the attack. Pallor of the face, of the tip of

the nose (Roberts), or of the ears (Ferber) previous to the attack yields, during the attack, to congestion of the face and head with an elevation of temperature, hyperemia, and fear of apoplexy.

Toward evening and at night these symptoms connected with the upper mucous membranes usually cease, so that sleep is seldom disturbed by them. As observed by Cornaz, an exception to this is the continuance of the secretion from the nose, so that the patient is obliged to sleep with a handkerchief under his cheek. The symptoms return regularly the next day, and usually with increased intensity.

These catarrhal symptoms and the extraordinary irritability of the mucous membranes remain; or, according to the age, sooner or later, after days and weeks the irritation extends into the chest, producing an aggravation of the disease.

Tickling or itching underneath the sternum, hoarseness of the voice, and a sensation of constriction throughout the chest usher in the dyspnea, which continues pretty regularly for several days or weeks, or gives way toward evening to a violent asthmatic attack, lasting till midnight or later.

The dyspnea is accompanied often only by a little cough, which occasionally breaks out into a barking attack simulating pertussis. It is usually associated with a scanty expectoration, yet sometimes this becomes profuse, and is then of a clear, watery, salty character. It is only in the late stage that a globular, stained, or pearly-gray sputum appears. At this time the whole mucous membrane, from the larynx to the bronchioles, may be the seat of a true inflammation, while during the principal stage at most merely a laryngobronchial catarrh exists that could be called catarrhal bronchitis only by those "who employ the termination -*itis* rather freely" (Phöbus).

The dyspnea is, as a rule, purely expiratory. The patient sits with expanded chest, from which the air is forced only by an effort in a long-continued expiration, while inspiration is carried on with customary ease, or even more readily. The inferior border of the lungs extends lower, and the apex of the heart is pressed somewhat forward. After continuing for some time, the patient becomes accustomed to the dyspnea.

At the beginning of the asthmatic paroxysm, which, as a rule, comes on in the evening, though it may appear at any moment as the effect of an external irritation, the patient finds himself restless. He changes his posture or place, seeks the window for fresh air, and returns again to his seat. This uneasiness rapidly increases to torturing anxiety. The movements of the thorax suddenly stop in extreme

inspiration. The patient sits motionless, propped by his elbows, or he leans over a table, the back of a sofa, or the foot of a bed. Lying is impossible. He remains thus, striving for air, till midnight or dawn brings quick recovery or gradual amelioration, unless toward the end of the attack a severe irritative short cough appears, to rob him of the remainder of his rest.

With the setting-in of the dyspnea and the asthmatic attacks every occupation becomes repugnant to the patient, who hitherto has had at least a tranquil time, every movement difficult, and often impossible. Stairs must be ascended slowly and with frequent interruption. The voice becomes feeble, the speech broken, conversation painful. The patient loses all desire for amusement, and if he does seek company, it is only to relieve his anxiety, and then he sits apart from the others, alone.

Exceptionally, the orthopnea continues for days. Blackley reports one case lasting with unabated severity for twelve days and nights.

In young people a copious secretion in the bronchi may increase, and so keep up the dyspnea until expectoration relieves it, at least temporarily. In old age there may be no secretion, and then the paroxysm of dry asthma becomes a principal complaint.

Ordinarily, in the yearly attacks the individual organs are affected in a descending series from the eyes to the chest. Rarely do they begin with asthmatic trouble, although when they do, the irritation extends in the reverse direction.

Fever may be entirely absent, and usually occurs only at the height of the disease. This period is reached in from several days to a few weeks, and continues for from eight to fourteen days under the domination of a mild remittent fever or an atypical febricula. The temperature seldom goes above 38.5° to 39° C., unless the bronchi become inflamed, when a higher degree may be reached. During the acme the general relaxation and uneasiness, sensitiveness to light and noise, and apathy to intellectual and agreeable impressions are greatest. Chilliness or burning of the skin, itching between the shoulder-blades or down the back of limbs, a feeling of irritation in the stomach, flatulence, and constipation may or may not appear. The pulse during repose is usually small, feeble, and slightly accelerated; but on movement and during excitement, it is often frequent and irregular, and during the not rare attacks of palpitation, impalpable. During the asthmatic attack it may become very slow.

Metabolism appears in most cases to be markedly disturbed. Gor-

don, Schmitz (quoted by Phöbus), Phöbus, Leflaive, and others, mentioned the scanty quantity of urine. Herbert asserts that a sediment of urates in the urine is frequent. Leflaive reported the uric acid to be double in amount during the attack, and called attention to the large amount of indican in the urine. More recently, A. Haig, Bishop, Tyrrell, and Kinnear reported the presence of uric acid in the blood.

Unfortunately, we do not possess an accurate analysis of the urine in hay-fever patients. The only one I found was done by a "professor of chemistry," treated by Phöbus on the worst days of a not severe attack that was cured by quinin.

The quantity of urine on five or six days averaged, "without the stool urine," only 1000 gm. daily. It was usually clear and light yellow, of a feeble acid reaction, and contained a small sediment of uric acid.

	AVERAGE FOR TWO DAYS.	
	During disease pro mille.	During health pro mille.
Solid constituents............................	75.0	79.0
Ash of these	24.0	26.5
Water	925.0	921.0
Urea	34.0	36.0
Uric Acid	1.3	1.6
Extractives	15.0	18.0
Albumins	0.25	0.5
Chlorids	8.5 ⎫	
Sulphates	7.2 ⎬	23.0
Phosphates..................................	4.7 ⎪	
Ammonia	Trace ⎭	
	995.95	1000.1

The most important result of this analysis is the considerable increase of uric acid both during the attack and in health.

During the principal stage, the duration of which is commonly from three to four, but may be twelve weeks, individual symptoms exhibit, as a rule, regular daily variations, so that photophobia and irritability of the nose are greatest during the morning, conjunctival irritation greatest during the evening, and the increase of dyspnea or coming on of an asthmatic attack almost always later. Yet these natural exacerbations and remissions are often disturbed by the action of external irritants, toward which patients during the critical period are exceedingly sensitive. The smallest causes, which would have absolutely no effect on the organs in health, now suffice to call forth an endless

attack of sneezing, a downpour of tears, an intense orthopnea, and produce again an inflammatory condition on the mucous membranes scarcely yet recovered from a previous attack.

Dry air, wind, a storm, a walk in the sun, over a meadow, going into another room, the opening of a window, the movement of a fan, the turning of the leaves in a book, dust from a carpet, the scent of flowers, the reappearance of the sun from under a cloud, a dazzling light, touching of the nose, the slightest alteration in the humidity of the air, a change in position, and many other things which will be mentioned in more detail among the causes of the attack, may at any moment transport a patient from a bearable to a most pitiable condition.

In a patient mentioned by Phöbus, for example, the sneezing attack came on so violently, on going into the sun, that he lost his hat, and could scarcely find the time to pick it up again.

Elliotson relates, from the notes of a physician in Bristol, the following: " Last week I was whiling away a couple of hours with some ladies and gentlemen in a hay-field, when suddenly all mirth left me, I cared not for wine or games, and was only happy to be able to conceal in a corner of the park the streaming eyes, flowing nose, and stormy sneezing, so as to protect myself from sympathizing witnesses."

Elliotson relates, again, the case of a woman who had to be carried twenty miles back to town from the country, where she was visiting.

The sensitiveness may be so extreme that physical impressions will produce an attack, from which is to be inferred how much of the hysteric element may come into play in individual cases.

Phöbus reports the case of a professor of chemistry, forty-one years of age, physically and mentally strong, a victim of Bostock's catarrh since his sixth year, whose symptoms were aggravated by seeing his own swollen face in a mirror, or by thinking of his disease.

Down relates another case, of an Irish girl, twenty-five years old, somewhat hysterical, and a sufferer from summer catarrh for seven years, who visited, during her critical period, an exhibition of paintings in London, and having gazed a little earnestly at a picture of a harvesting, she was suddenly attacked by violent symptoms that necessitated her departure from the exhibition.

Convalescence, which follows the acme, is, as a rule, gradual, and the symptoms disappear in the order they came on, rarely in a reverse order.

An after-stage frequently exists, inasmuch as, following the cessation of all local symptoms, an inclination to a relapse of the sneezing paroxysm or the asthma, etc., under the influence of special causes, remains for some weeks, associated with a general weakness and in-

creased irritability.   The first frost often brings the autumn catarrh in America to a sudden termination.

As to *complications*, we find now and then mention of migraine-like headaches, neuralgia of the supra-orbital nerve and other branches of the trigeminus, salivation, vertigo, and sleeplessness.   Urticaria, eczema, and other skin affections seem to stand in close connection with the disease, or may be, rather, with the constitution of the patient, but we will return to these.   Edson and Beard report paralysis of the diaphragm, Beard spasmodic stricture of the esophagus and aphonia during the attack; but we know not if these "hay-fever cases" were genuine.

Combinations with other diseases may occur, in as far as patients with Bostock's catarrh ordinarily show a hereditary predisposition to nervous and "arthritic" affections.   On this point, more under the heading of Etiology.   The association of the disease with emphysema has been often reported, and both were aggravated thereby.   Several writers insist that pulmonary tuberculosis and summer catarrh are never seen together.

As *sequelæ*, conjunctivitis, otitis media, otitis externa, and pharyngosalpingitis have been now and then mentioned.

Germain Sée stands alone, as is not uncommon, in his report of the occurrence of heart failure with dropsy in the tenth year of the disease.

DIAGNOSIS.

THE diagnosis of Bostock's catarrh is easy, if its characteristics are considered, not one by one, but in connection with one another. It is certain in those cases where for a series of years a typical recurrence of the characteristic attack is seen. But even the first attack, when reasonably well developed, especially if it occurs in the descendants of hay-fever patients—and this hereditary appearance of the disease is, as we shall see, not infrequent—even the first attack under these circumstances should not easily be overlooked.

In the first attacks the differential diagnosis must always be made between it and masked intermittent fever, which manifests some similarity with it. Moreover, in atypical cases the observations of George Johnson must not be forgotten, in which a chronic arsenic-poisoning by green tapestry, with symptoms of headache, cold in the head, digestive disturbances, and finally asthma, was treated for a long time under the diagnosis of hay-fever.

I personally have seen two young ladies mimic, with flowing eyes, running nose, and dyspnea, for a whole summer the genuine hay-fever of a cousin, till a touch of the galvanocautery behind the ear cured them, but not the cousin; and I must confess that during the first week I believed it to be Bostock's catarrh, and not hysteric imitation. The second diagnosis was proved correct when, a couple of months later, the "Nona" which the newspapers reported as a specter appeared to the younger of the two for two days, and, further, when a hysteric aphonia, manifesting itself now and then, set in during her engagement. She and her sister are to-day happily married, and have never since had a second attack of their pretended hay-fever.

In the differential diagnosis it must also be remembered that, although, as a rule, Bostock's catarrh begins in early summer, and usually in June, it is not rare to see *the same form of malady in individual cases at other definite seasons, so that there is no reason for considering the catarrh as an absolutely spring, summer, or autumn one.*

Yet a variation in the season is sufficient to arouse caution in the diagnosis. There are, for instance, quite a number of cases in which erratic attacks of an ordinary nervous asthma, or nervous coryza, took on a periodic character from the accidental yearly recurrence of something noxious to an idiosyncratic individual; which might, therefore,

be taken for a typical annual catarrh. Apart from the short duration and anomalous course of the attack, a differentiation might be made in very deceptive cases by the fact that the individual can bring on the attack by his voluntary approach to the noxious influence outside of this definite time.

The following abstracts from observations by Molinié are pertinent here: A hairdresser who dusted ladies' hair with iris powder at carnival time was always tormented at this period with continual attacks of sneezing, accompanied by a defluxion from the eyes and nose. A druggist who every June received and worked over large quantities of roses for pharmaceutic preparations experienced always at this time, while the roses remained fresh, an intense coryza associated with attacks of sneezing. The yearly return of a pseudo-summer catarrh we also find in the following case by Molinié: A corpulent man of arthritic family, who later became affected with diabetes mellitus, was attacked in his fortieth year, for the first time, after eating strawberries, with an urticarial eruption of the face and neck, accompanied by violent sneezing attacks and an extraordinary watery discharge from the nose and eyes. These symptoms lasted from three to four hours (!) and then disappeared. The attack recurred every succeeding year under the same circumstances, till toward the age of fifty, when they passed away. His maternal uncle suffered in the same way after eating cherries, and a female cousin, after eating fresh or cooked sorrel.

A fourth observation of the same author is interesting, for, although there would be no fear of confusing the case with Bostock's catarrh, it furnishes an example of a "weekly type," in contrast to the "yearly types" already shown: A young man, who was in the habit of taking a Sunday walk into the country, suffered from a "Sunday cold" until he learned to give up his little excursion.

The following cases serve as a worthy supplement: Two men, one a notary, aged forty, the other a druggist, aged thirty-five, could never approach their mother-in-law without an attack of sneezing and coryza; in other words, an asthmatic paroxysm. Investigation proved that for one the odor of camphor in the room was the cause; for the other, the lycopodium dusted on the intertrigo of a grandson cared for by the old lady.

Confusion with emphysema, on account of the increase of its symptoms at the beginning of summer, seems scarcely possible, yet it has happened (Phöbus).

The epidemic or endemic occurrence of a group of symptoms appearing similar to typical summer catarrh shows a criterion in the very number of its cases which prevents confusion with the, at most, sporadic occurrence of Bostock's catarrh. Consequently, only for the sake of completeness, I mention, with Phöbus, an epidemic catarrh with fever which, according to Braun, occurs in Venice every spring, attacks numbers, continues for months with exacerbations and remissions, is unfavorably influenced by sunlight and favorably by the moist sirocco with rain or cloudiness.

ETIOLOGIC FACTS AND OPINIONS.

THE number affected with Bostock's catarrh is comparatively insignificant. From the discoverer's first communication to the time when Phöbus instituted his careful and extensive investigation as to the occurrence of the disease,—therefore, in almost half a century,—there were, at most, 300 cases to be found in Europe. Since then the number of cases has increased, and so considerably that we must allow a rise in morbidity, and not ascribe it alone to greater carefulness on the part of the physicians. Undoubtedly, the number of so-called cases is to-day exaggerated, for a great portion of them in the literature of the last thirty years have nothing in common with Bostock's catarrhus æstivus.

The origin of the disease is veiled in obscurity. There is not the slightest support for placing its occurrence before Heberden's time. If history can at all be trusted, the disease must have originated through the concurrence of unknown circumstances, about the middle of the eighteenth century, and from a gradual, slow growth in frequency, it has become more rapid.

The first known case of an annual summer catarrh, as we have already mentioned, was seen by Heberden after the middle of the eighteenth century. Bostock's first attack took place in 1781, and a female patient of Elliotson laid the beginning of her disease in 1798. Phöbus found, from the reports sent to him, about seven British and three Germans whose attacks began in the eighteenth century. In view of no earlier communications, we must face the question, Did the disease actually arise in the middle of the eighteenth century, or was it up to that overlooked? Some English writers, believing in the dependence of the catarrh on the aroma of certain plants, asserted that the introduction and dissemination of certain grasses in England was responsible for its origin. As a matter of fact, the Lolium italicum, and other meadow-grasses, were first transplanted to England about that time; though Gordon, Elliotson, and others ignore these fodder-grasses, and blame the Anthoxanthum odoratum, which existed in England a long time before. Since, as we shall see later, the Anglo-Saxon race possesses a predisposition to catarrhus æstivus, and since history shows in other cases that predisposed races may be brought into contact with a noxious influence carried from a distance, only after it has existed for a long time, and may thereby exhibit quite a new disease, there is no good reason for rejecting Heberden's time as the period of origin of Bostock's catarrh, especially if the hypothesis to be discussed later should be confirmed—namely, that the disease is caused by a living germ. Another fact, also, as mentioned by Phöbus, speaks for the late origin of Bostock's catarrh

—namely, that it would be unintelligible how the older physicians, who paid such attention to the typical recurrence of diseases, and frequently recorded it in cases where we no more see it, could overlook such a striking recurrence as the disease manifests. In fact, among the many "febres intermittentes annuæ" and "febres anniversariæ" described by Tesla, Rayer, and Mongellaz, there is no annual summer catarrh, although they mention a birthday fever, "febris natalica," as a yearly ephemera in certain patients.

Yet when and wherever hay-fever first appeared, it is now certain that, though rare on the Continent, and especially in Germany, the number of cases in England and the United States is on the increase, and in these places, where the disease seems to find a soil suitable for its development, it threatens to become endemic.

Of 154 cases collected by Phöbus up to 1862, 80 were Englishmen, 34 Germans, 14 French, and 9 Belgians. At this time but little was heard from America with regard to the disease. There are to-day in Germany many experienced physicians and clinicians who have never seen a case of genuine hay-fever, while in London almost every physician knows several cases, and in North America the number was estimated at more than 50,000 twenty years ago. The best of the recent German text-books on special pathology and therapeutics make no mention of the disease or give it only a passing notice. It is not found in Niemeyer's text-book, or Liebermeister's lectures. Kunze, Strümpell, Eichhorst, and others seem to know hay-fever only in the sense of an idiosyncrasy to plants in bloom. I personally have seen but four undoubted cases since Rühle showed me the first one thirteen years ago, and I have heard of but about the same number. The best proof of the frequency of the disease in the United States is the Hay-fever Association, which was founded at Bethlehem in 1874, and of which all sufferers from either of the two forms of the disease, rose-cold in June or hay-fever in September, may become members. According to von Hensinger's report, there are also honorary members. Bethlehem is a town in New Hampshire with an elevation of 1450 feet above the sea, where the patient is protected from his summer catarrh, provided he arrives there before it has set in and remains till the commencement of cool weather.

In the countries where the disease is most common there are, again, districts of predilection. Thompson and Morell Mackenzie report that it is more frequent in the south of England, especially in the neighborhood of the Bristol Channel, than in the north and east. And Wyman reports numerous cases from Cambridge; Waters, from Liverpool. According to Hirsch, the North American zone of hay-fever is pretty sharply defined; it runs eastward along the Atlantic seaboard from Virginia to Eastport (Maine), and westward along the Mississippi River. Beard, Wyman, and Patton report not a single case from the districts lying northward of the St. Croix River and the Great Lakes, from Canada, New Brunswick, Nova Scotia, etc., and only exceptional cases in the western and southern portions of the United States. The tropic and subtropic countries of America, especially California, never see the disease.

Guéneau de Mussy, Leflaive, and Molinié regard the disease as well

known, and yet not common, in France, and particularly in Paris. It is at least more frequent there than in Germany.

Since Phöbus's time, isolated cases have been reported from Switzerland, Spain, Italy, Russia, and Scotland. Morell Mackenzie mentions one or two from Norway, Sweden, and Denmark; Semon and Glas, one from Sweden. No case has been found in Ireland. The Irishwoman mentioned by Dr. Down lived in London.

[The statement as to the exemption of Ireland from hay-fever needs qualification. The editor knows of his personal knowledge two instances at least. One case is that of a physician and surgeon residing in a midland county who suffers severely every June—indeed, to such an extent that he has been obliged to make almost yearly pilgrimages to the Isle of Man to escape or abort an attack of what to him is a veritable plague. The second case is that of a clerygman, who suffers at precisely the same season to a greater or less extent every year. This gentleman has studied his symptoms and their cause with care, and is convinced in his own mind that the affection has a microbic origin.]

Blackley asserts the occurrence of the disease in the temperate Himalayan climate of India. In general, Asia, Africa, Polynesia, and Australia are free (MacDonald). Only William Smith, who mistakes the conception of true hay-fever entirely, reports a combination of it with malaria in New Zealand, Australia, Hindostan, Farther India, and other Asiatic countries.

In all lands where the disease occurs it is always less frequent in the country than in the city; less frequent and milder on the sea-coast and in woody, mountainous regions than between them, especially in agricultural districts. Yet its course for any single patient is, according to the majority of writers, milder and shorter in the city than in the country. Moreover, the air of closed rooms is better borne than that in the open. An ocean voyage gives almost absolute protection from the annual attack.

Besides the open sea and the northern and southern portions of the earth, there are a number of countries and districts in the temperate zone that are immune in the sense that hay-fever does not exist endemically, and sufferers who arrive from other places are protected against attacks during their stay. With a great reputation in this regard we find, in America, Louisiana (Patton); further, Fire Island on the Atlantic coast of Long Island; the Island of Long Beach on the coast of New Jersey (Ashhurst). The White Mountains, the Green Mountains, the Catskills, and the Adirondack Mountains have sanatoria (Wyman and Beard). Overlook, the highest point of the Catskills, is, according to Blackley, especially sought by patients before the critical time. In England, Lundy Island in the Bristol Channel, the Lizard in Cornwall, St. Mave near Osborne, and several islands on the west coast of Scotland are considered immune.

In the geographic spread of the disease the striking predilection for the Anglo-Saxon race is evident. Beard's remarkable report confirms this marked predisposition of Englishmen above all others, even above those from the same lineage: While summer catarrh is very frequent among the English citizens of New York, Dr. Jacobi, whose practice is predominantly among the Germans, has never seen this disease among them; and Dr. Chauveau, whose clientèle is drawn from the French inhabitants, affirms the same.

As to the predisposition of sex, Bostock, and every writer since him, report a greater frequency among men than women.

Phöbus	found	out of	154	cases,	104	men	and	50	women;	
Wyman	"	"	101	"	72	"	"	29	"	
Mackenzie	"	"	61	"	38	"	"	23	"	
Molinié	"	"	42	"	25	"	"	17	"	
Therefore		"	358	"	239	"	"	119	"	

or *two* men to *one* woman. Beard, whose notion as to the limits of the disease is somewhat confused, puts the proportion at 3 to 1.

The disease is called, with reason, an aristocratic one, since it moves almost exclusively in the best circles of society.

Literary men, physicians, the intellectual, officers, nobles, merchants, are most commonly attacked. Among 154 cases, Phöbus found 16 (possibly 19) physicians, and only 8 from the laboring class, of whom 1 was a North German coachman, 1 a saleswoman from central Germany, 2 English workmen. Ferber, who was a sufferer himself, had among 700 factory-hands on his ledger no case of hay-fever. Morell Mackenzie counted 61 in his private, none in his hospital, practice. Blackley saw 48 cases, all in educated people; Wyman, 55, and only 6 uneducated among them. Smith alone, of whom we have already said that he was unable to diagnosticate the disease, reports that "poor people, too, suffer from the disease in public hospitals."

That dwellers in the city are more predisposed than those in the country has been already mentioned.

Beard counted among 200 collected cases, only 7 country-people, landed proprietors and farmers. After much inquiry among these same people, Blackley found cases only exceptionally.

A hereditary predisposition has been proved with marked frequency, considering how rare the disease is.

Of 56 cases, about which Phöbus obtained authentic information, 33 showed the disease in near relatives. Molinié found a direct heredity in 6 cases out of 42, and several times an inclination in the parents to nervous coryza. Wyman had in one family 6 patients; in another, of 6 people, 5 sufferers.

The conclusion that a certain *constitutional anomaly* underlies the individual predisposition to Bostock's catarrh is becoming more and more positive. Moreover, it can now scarcely be denied that this diathesis is what the English and French call the arthritic, which expresses itself in the hereditary predisposition of families to rheumatism, gout, diabetes, corpulency, migraine, furunculosis, bronchitis, asthma, etc. Bostock himself called attention to his own gouty habit, and Phöbus found the same in many patients; yet Guéneau de Mussy (1868) was the first to bring forward this diathesis as a necessary basis for the disease, and his teaching was confirmed by the addition of new material from the observations of Herbert, Leflaive, Lermoyez, Ruault, de Dreyfus-Drisac, Rendu, and Molinié. Molinié (1894) demonstrated the arthritic constitution in all of his 42 patients, and in 8 of them the particular manifestations of rheumatism, gout, and corpulency. In proving "lithemia" in Bostock's catarrh, A. Haig, Bishop, R. S. Tyrrell, and Kinnear consciously or unconsciously confirmed Guéneau de Mussy's hypothesis. It is probably, then, no accident that the aristocratic Bostock's catarrh, as well as the "morbus principium" of Sydenham,—in other words, the gout,—should show a predilection for the Anglo-Saxon race.

The *neuropathic tendency* of summer catarrh patients is proved in several ways, as nervous disease in the patient himself, the occurrence of nervous disease in his family, and the previously mentioned alternation or combination of the disease with urticaria. Many patients— *e. g.*, Ferber—expressly report the existence of asthma nervosum in near relatives; others, a predisposition of themselves or relatives to erythema, nervous palpitation, or gastralgia. These facts become easy of comprehension on account of the intercommunication of the roots, as brought out by Thariot, between arthritism and the famille névropathique.

There is still the further question, however, whether the general disease finds its local expression in a particular anatomic condition of the affected organs. Many have disposed of the question by simply answering in the affirmative, as if the predisposition to the disease was to be sought without further investigation in a *local anomaly of the upper air-passages.*

According to MacDonald, the aquiline nose is popularly considered an attribute of hay-fever patients, and in isolated cases a large nasal cavity, a defective Schneiderian membrane or one abnormal in function has been looked on as the cause.

Daly, in Pittsburg (1882), was the first to point out the abnormal sensibility of a diseased nasal mucous membrane as a sufficient cause of hay-fever. Isch Wall at once insisted on the thickening of the mucous membrane by hypertrophy and congestion as the reason for this increased irritability. Sajous (1883) based his explanation on the theory of "zônes hyperesthésiques"; yet while he put these zones on the septum opposite to the middle turbinated bone, Sandmann found them on the anterior portion of the middle turbinated bone itself, in the region innervated by the nervus ethmoidalis, and Moore and Ruault would make the whole nasal cavity the site of increased irritability. Hack (1883), of Freiburg, found the local predisposition in a marked swelling of the corpora cavernosa in the erectile zone on the anterior portion of the lower and middle turbinated bones; and many of his pupils reported a pronounced hyperemia and sensitiveness to touch at this situation, pressure on which usually produced an attack of sneezing. John Mackenzie, on the contrary, attributed the blame to the mucous membrane of the posterior portion of the lower turbinated, or, in other words, the region of the sphenopalatine nerve in contrast to that supplied by ramifications from the ophthalmic branch of the fifth. According to Roe and Richard H. Thomas, hay-fever is always associated with a demonstrable nasal affection, whether it be a polypus, or hypertrophy of the mucous membrane, or some other obstructive anomaly; as H. Allen also had already affirmed that an occlusion of the nose was always to be found, the removal of which would cure the disease; but all these, from Daly to Thomas, throw hay-fever, nasal asthma, paroxysms of nervous sneezings, etc., together. Molinié, who makes a clearer division of these forms of disease, observed the nasal mucous membrane manifestly altered in only 22 out of 42 cases of summer catarrh, and Böcker called attention to the fact that among 300 cases of mucous polypi of the nose, only 9 suffered from "dyspneic attacks," and not one of these was cured by the removal of the polypus.

In general, it is evident that, like every laryngologist in whooping-cough, so almost every rhinologist observes something different in hay-fever, and each one is successful in treatment corresponding to his own hypothesis, though other physicians may try it in vain.

The same differences in opinion, seen in reference to the local predisposition, are to be found again in the consideration of the *exciting external causes*. Immediately after the discovery of the disease, there was a divergence of views. Since all are supported by facts, observed by trustworthy investigators, we feel obliged to mention them.

Bostock himself found the external excitant of his malady in the early summer heat; and Phöbus, Guéneau de Mussy, Déchambre, Kinnear, and Beard followed him. The physicist Hermann von Helmholtz, and the physician B. Ferber, assure us that heat at least made their condition worse.

Helmholtz reports, after twenty-one years of personal experience, that his affection ameliorated in cool weather and rapidly increased in

severity under the influence of heat and direct sunshine; moreover, in a cool room the symptoms disappeared as quickly as they came.

Ferber, who "from his seventh or eighth year had the melancholy pleasure of suffering the more severely, the more beautiful the May and June," asserts that he always found "most unbearable the effect of the sun: a short distance without shade or only the dallying to speak at a sunny street-corner was sufficient to produce at once an attack of sneezing. Not less injurious were differences in temperature. Let me enter a cool room after a quick walk, and I could scarcely speak from sneezing. Drafts affected me in the same way. . . . I have never observed, as the majority of patients assert they do, any bad effect from the smell of hay or any other odoriferous substance, although on account of my surroundings and the duties of my daily life, I meet with sufficient opportunities. On one single occasion this summer the scent of the bitter-sweet growing in my garden irritated me so as to bring on repeated sneezing attacks with subsequent aggravation of symptoms. . . . Flashes of light—as, for instance, the seeing of lightning at night—had no effect."

George M. Beard also, as well as many others, lays great stress on heat in the causation of an attack, and expresses the opinion that the disease should be called *sun-fever*, not *hay-fever*.

That heat, even in susceptible individuals, is not sufficient to produce the disease, is evident from the fact, confirmed by numerous patients and physicians, that in tropic regions some patients escape their annual attack, provided they betake themselves thither in time.

We have seen that the name hay-fever or hay-asthma stood as a popular term for Bostock's malady in England at the beginning of the last (nineteenth) century, and that the writers following Bostock, supported by the assertions of their patients (Elliotson, in fact, supported by experiment), defended the etiology which lay at the base of this designation, either in a broad or narrow sense. The increase in the nervous irritability of the patient before the hay period, the outbreak of the catarrh with this, the immediate aggravation of all symptoms on approaching a meadow or a haystack, the remission of the symptoms with cool weather, are the facts (allowed to-day, even though we explain them otherwise) on which the name hay-fever was based. It was not long before we heard that it was not so much dried hay, as fresh hay, and not only not this, but hay in bloom that was injurious. Examples, like the one related by Phöbus, of the woman whose attacks began two years in succession on the reception of a bouquet of grasses and wild-flowers, became numerous and were repeated in every conceivable way. In the mean time certain inquiring minds began to examine what emanations or effluvia of hay or grass could be made responsible for the symptoms, and what grasses or plants were to be regarded as excitants. Some said it was the dust of the hay; others,

the odor of grasses and flowers; others, still, the pollen, that produced the irritation. While the discussion was going on over the different substances that produce the scent in hay or flowering grass, over the different grasses and other plants that discharge their pollen at the critical period of the year, besides these supposed excitants a whole series of other causes capable of producing hay-fever sprang up. Before introducing a short table of all these excitants, I intend to give an example of the frivolity observed now and then in the determination of causes. A celebrated case referred to by almost all recent writers on hay-fever as a remarkable instance of peculiar causation is that of Charlton Bastian, in which the "emanations" from a horse parasite, the Ascaris megalocephala, were made responsible for the disease.

Turning to the original communication, the reader is surprised that the zoologist Charlton Bastian describes the regular picture of Bostock's catarrh, attacking him two years in succession in May, and lasting six weeks, "because" he examined anatomically at this time, and only at this time, ascarides fresh and preserved in alcohol. Yet since he came in contact with this object at no other time during the year, and since we know nothing more about the history of the patient, the most we can do is put the case on record as an example of a remarkable idiosyncrasy, and raise a warning against a perpetuation of a wrong conclusion on the part of a zoologist unacquainted with Bostock's disease.

Consequently, the following list of all the "causes" may be taken with reservations, though they have been stated by writers or their patients usually as excitants, or at least as aggravating irritants, in summer catarrh:

Hay.
Meadow-grass.
Fodder-grass.
Rye (Phöbus).
Bean-blossoms (James Bird).
Roses.
Limes (A. Smith).
Cantharis.
Jasmine-blossoms.
Mangifera (Gordon).
Nettles (Simpson).
Seaweed (Gordon).
Maize-blossoms (Deacke).
Grain in general.
Rice (Cornaz).
Peach-blossoms.
_____

Decoction of flaxseed.
Ipecacuanha.
Tea.

Street-dust.
Bed-dust (Longueville).
_____

Heat (Bostock).
Cold (Smith).
Bright light [sun, gas, petroleum; electric light is harmless (J. Bloom)].
Ozone.
Vapor of burning sulphur.
Emanations from hares, rabbits, calves, young pigs, cats (Wyman).
Odor of roast hare (Thorowgood).
Frequenting concert-rooms, dance-halls, theaters, restaurants, or railroads (Hack).

It seems to me that two different conclusions may be drawn from this series: First, that the laity and certain short-sighted physicians very readily confuse exciting and aggravating causes; second, that, as a matter of fact, there are a great number of different irritants which produce or increase the symptoms of Bostock's catarrh in different people. Moreover, when we consider that the authenticity of many of the cases of hay-fever in which the enumerated irritants played a rôle must remain in doubt, it is well, with regard to the overwhelming majority of the writers who knowingly adhere to the name "hay-fever," to look away from the "causes" which are most quoted and to consider the following facts, stated by Phöbus after a careful analysis of his cases as most likely to be true in relation to the influence of different grasses: "Especially active are those grasses that either give off a large amount of pollen (rye) or smell very strongly, and either of these during the first heat of summer." Phöbus himself indicated the means by which the significance of pollen as a cause in aggravating the disease might be proved: he insisted on the microscopic examination of the air, and of the catarrhal excretions of the patients. Small glass slides of certain size, coated with a sticky material, set in the air for a definite time, would demonstrate the precipitate from the air.

No one expended so much energy and diligence in working out this method and carrying to a further issue Elliotson's earlier experiments on the irritative effects of pollen as the homeopathic physician, Harrison Blackley, in Manchester, whose "Experimental Researches" appeared first in 1873, followed by a second communication in 1880. This work was for a long time overestimated as a solution of the question of the etiology of hay-fever; yet it will always remain as an important addition to our knowledge of one of the irritants capable of aggravating hay-fever.

Blackley showed that the disease was most severe in himself and his patients at the period when the air contains the greatest amount of pollen; that it more frequently exists in the country, where the air contains more pollen, than in the city; that it is milder on cool, that is, rainy days, when the amount of pollen in the air is less, than on hot dry days. He therefore drew the conclusion, at which Phöbus had previously hinted, that Bostock's catarrh was a "pollen catarrh."

He estimated the amount of pollen in the air at low levels and at high elevations, and found that in the highest regions which he was able to reach with a paper kite the pollen was much greater (!) in amount than on the level. He states exact figures as to how much pollen must be deposited in twenty-four hours on a small glass plate a

square centimeter in size before there is sufficient in the air to affect any one, and he states, for instance, that for himself 20 granules are required; that for another, 25 is the minimum; while 54 to 60 granules of pollen constitute a signal for severe attacks.

More important than all this are the direct experiments with pollen conducted after Elliotson. He demonstrated that the inhalation of pollen into the nose irritated intensely those afflicted with the disease, while it had no effect on the healthy, and that the conjunctiva is very sensitive to the infusion of a pollen decoction (from Gladiolus) during the critical period. Again, he inoculated the scarified skin of patients with pollen (of the Lolium italicum), and found after several minutes of intense itching, edematous swelling of the subcutaneous connective tissue, reaching the size of the palm of the hand and $\frac{3}{4}$ inch thick, without pain, heat, or redness. His results as far as the critical period of patients is concerned were confirmed by Farrar Patton, working under the direction of Binz, and by Elias Marsh, who experimented on himself as to the effect of pollen on the nasal mucous membrane. The irritative action of pollen on the skin might have been already learned from a communication of Elliotson, probably overlooked by Blackley, in regard to a woman afflicted with hay-fever, whose hands inflamed every time she came in contact with meadow flowers.

Blackley showed, further, that pollen from fresh blooming plants was more effective than from the old and withering; and that the pollen of poisonous plants—for instance, the Atropa belladonna—had no more a qualitative effect than the non-poisonous.

Blackley convinced himself by microscopic examinations of the most active pollen that the size and form, roughness or smoothness, of the granules made no difference, since he found very varying peculiarities in equally effective kinds. Moreover, the amount of mineral matter in the pollen—suggested by Thomas Harrison after investigation with the spectroscope as to the sodium and barium salts in the pollen of Lolium perenne and Secale cereale, two very effective kinds— makes no difference in the irritative action. He evidently overlooked a conclusion of Phöbus in regard to this—namely, that the chemical composition of the effluvia of hay is not inactive. These effluvia attack especially roof-tiles, and gradually cause them to become soft and brittle, so that well-burnt tiles that ordinarily last three hundred years or more become useless over a hay-loft after, at most, thirty years.

It is needless to enumerate here all the different kinds of pollen which Blackley and others collected, counted, weighed, analyzed, and,

with or without sufficient evidence, found more or less responsible for the disease. Suffice it to say that every kind of pollen from seventy-six different natural families of plants could produce in the susceptible an attack at the critical period; pollen from the Graminaceæ most readily, that from the Phanerogams least readily. Let us add that different patients complained of different pollen; that in different countries, different plants and different kinds of pollen were accused; that there are and were many patients and physicians who deny the pollen theory entirely, and that Blackley himself eventually allowed that there were other agents besides pollen capable of producing "symptoms similar to hay-fever."

Blackley himself, Beard, and Molinié, all mentioned the fact that different patients complain of different pollen. Beard (1876), who, like Phöbus, employed letters of inquiry and drew his conclusions from 200 cases in the United States, found more than thirty different irritating substances, and names as the most important excitants dust and heat, and he insists that different patients manifest a varying, but for them specific, sensitiveness to different noxious substances.

Molinié found pollen an effective irritant in only 6 out of 38 cases, and that in individual cases stored hay was active even at other seasons. Four of his patients complained of walks in the fields, two of the scent of roses, twelve of railroad journeys, four of passage from shade to the sun.

In North America Wyman and Elias Marsh attribute the irritation exclusively to the pollen of Ambrosia artemisiæ folia (hog-weed). The plant is not seen in Europe, and blooms in the United States from August to September; that is to say, during the months of the autumnal catarrh. Yet W. Smith insists that timothy grass, and Lockwood, of New Jersey, that rag-weed is the most irritating plant for North Americans; and others, again, blame maize. In England the most provoking pollen is from the Anthoxanthum odoratum, the Holcus avenarius, etc.; in Germany, from the Secale cereale, and likewise the Anthoxanthum odoratum.

How little agreement there was among writers as to the significance of pollen is quite evident from the statements in earlier papers, and how much the convictions of individuals are influenced by the theory predominant in their time is best demonstrated by the fact that, since the promulgation of the hypothesis attributing the disease to obstruction of the nose, the influence of pollen has waned, till John N. Mackenzie could say to the American Medical Congress in 1895 that he was happy to find no mention made of the pollen theory in the discussion of the etiology of hay-fever, for it only stood in the way of the proper comprehension of the disease.

Yet, in spite of J. N. Mackenzie and those who agree with him, pollen does play a certain rôle in hay-fever. It must only be remembered that two things are necessary to make it effective—a susceptible individual and the proper season; that it does not act on all patients suffering from Bostock's catarrh; and that, besides this, there are many other things capable of producing an exactly similar effect.

Moreover, it must not be supposed that every attack of sneezing or asthma produced by pollen is to be considered hay-fever, although pollen is the most important of all the noxious agents in inducing exacerbations on the typical disease.

For the inhalation of the most different kinds of pollen by the healthy is without result, as Elliotson, Blackley, Patton, and Zuelzer affirm, and as I have found from innumerable experiments on myself. The inhalation by hay-fever patients is innocuous outside the period of disease manifestations, as was proved by Allen Woodward, who kept plants in bloom on his writing-desk for weeks, so that the pollen covered everything around him, and who tried hundreds of different plants, yet remained unaffected until his critical time, the 20th of August. Moreover, the healthy, and patients outside of their attack, are insusceptible to pollen inoculation, as was shown by Blackley and Patton. Isolated exceptions, like those mentioned by Molinié, where stored hay was injurious to summer catarrh patients, even before their critical period, prove, at most, that a person may suffer from Bostock's catarrh and show at the same time an idiosyncrasy to the dust of hay.

It is unnecessary to refer here to how Blackley endeavored to divest agents mentioned by other authors (ozone, odoriferous substances, like cumarin, benzoin, etc., dust, light) of all irritative effect, after that he himself later acknowledged the possibility of the action of other agents and the difference in idiosyncrasy manifested by different patients.

One example will suffice to show how irrelevantly Blackley drew his conclusions: One summer day on a dry road he happened to be enveloped in a cloud of dust raised by a passing wagon, and he was immediately seized with a paroxysm of sneezing, which developed in a short time into all the symptoms of his summer catarrh. On microscopic examination of the dust taken from the middle of the road, he found nothing peculiar, but in that taken from the upper layer at the side of the road he found small polygonal pollen granules, with which he succeeded later in an inhalation experiment, having come on them again by accident. In a room of his house was a bouquet of wild flowers picked by his children. As he touched it a cloud of pollen flew in his face and he was seized with an attack.

His conclusion was: Since in one case the pollen probably excited the paroxysm, and in the other the dust from the road containing pollen granules, these, and these alone, are to be regarded as the excitants. For "the autumn dust that contains no pollen granules is indifferent to me." But he forgot to prove for himself, as Woodward has done, that pollen, too, might be inactive in autumn, and draw the more correct conclusion that he was sensitive to pollen and dust only at the critical period.

The statement of Blackley, Lühe, Pfuhl, Schmidt, and others, that pollen granules may be found in the nasal discharge of sufferers, but

not (!) in that of the healthy, must simply be brought into accord by its authors with the ubiquity of pollen.

Helmholtz (1868) asserted that he found during the annual attack in the nasal discharge a motile vibrio-like body, and he theorized that hay-fever was an infectious disease caused by this vibrio. This hypothesis received at the time full support from individual observers, especially Binz, who induced his pupil, Farrar Patton, to carry the investigation further. Patton found in the nasal secretion of a woman at the time of her attacks motile vibrios, which resembled so closely in form, size, color, and inclination to arrange themselves in pairs or in squares the fovilla particles from the interior of the pollen of Dactylis glomerata that uncertainty arose as to whether they were true vibrios, or not rather the transformation products (discovered in the mean time by Lühe in 1874, and later by Pfuhl in 1878) of pollen granules which had burst in the nose. It strikes me that but little judgment was exercised as to the assistance that would be given by the consideration of a living infection for the explanation of the typical course of the yearly attacks, if Helmholtz's theory and discovery were laid aside.

In *theorizing on the pathogenesis* of Bostock's catarrh, it is necessary to keep in mind all the symptoms of the disease, and all the assured facts that participate in its origin. For this the following may serve as a basis:

The limitation of the disease to a very small number of people living under the same conditions as thousands of others who remain free, its pronounced predilection for a certain class of society and for a certain race, its repeated appearance in members of the same family, the ineradicable tenacity with which it clings to life, the typical changes that it undergoes with years, sufficiently prove that the principal cause of its origin lies in the affected person himself. The name idiosyncratic summer catarrh, proposed by Biermer, refers to the necessity of an individual predisposition before the disease can occur.

Further, the typical course of the individual annual attacks, and the undisputed possibility of escaping them by avoiding certain local necessary conditions, point unquestionably to external exciting causes that must reach the susceptible individual before the disease can originate.

Further, the severity of the symptoms, their results and course during the attack, make it certain that an inflammatory irritation of

the mucous membrane is not the cause of them, but rather an excitation of the centripetal nerve tracts, the irritability of which has been raised, and this excitation is conducted reflexly to the glands and muscles of the affected organs. We must expressly insist that the first symptoms are not a primary inflammation of the mucous membranes with excretion of the inflammatory secretion, but a true hypersecretion of the glands, accompanied by vasoparalytic symptoms, and a true hyperkinesia of the irritated muscles, and all inflammation of these parts is secondary. From this point of view, rhinorrhea and bronchorrhœa æstiva (Scott, 1842) would be proper names, and not rhinobronchite annuelle (Leflaive, 1887).

After the mention of these facts, the questions still remain: Is the predisposition of the individual to the disease due to general or local causes?

Where does the exciting cause localize itself, and is it endogenous or exogenous in character?

Finally, is this excitant a physical or living irritant? in other words: in the yearly attack, are we dealing with a mechanical irritant, relatively a toxic lesion, or an infection?

We can answer the first question at once; for although the arthritic diathesis plays an evident and almost undisputed rôle in hay-fever, it is necessary to assume a particular local irritability of the eyes, nose, etc., in order to explain the marked difference between the small number of summer catarrh sufferers and the large number of those afflicted with arthritism.

This disproportion sufficiently disproves the extravagant assertions of individual pupils of Guéneau de Mussy, who added to the teaching of the master, at the sacrifice of common sense: "La diathèse est tout et les influences extérieures rien. L'asthme de foins est le produit de l'organisme seul. . . . une maladie permanente à manifestations périodiques, produit exclusif de l'organisme, maladie salutaire, maladie providentielle" (Herbert and others).

It was not at all unreasonable to seek the local predisposition in some peculiarity of the affected organs—a particular shape or size of their cavities, an especial anomaly in the mucous membrane covering them; yet every attempt to demonstrate and define such peculiarities failed. And it may be concluded *à priori* with certainty that every theory which makes the whole symptomatology dependent on an anomaly of a single part, like Daly's and Hack's nasal hypothesis, is incorrect. For the symptoms begin in the eyes, before the nose shows

the slightest participation, and they extend in the course of the attack downward in such a fashion as a simple nasal reflex would never do.

The writers who assert an anomalous condition or deterioration of certain centripetal nerve tracts have approached most nearly the pathogenesis that would accord with the facts. In this theory the sensory tracts from the conjunctiva, the nose, the throat, and the bronchi are taken into account, and the intense local paresthesiæ of these parts, which have procured for the disease the names pruritic catarrh (Stucky), itching nasal catarrh (Rumbold), rhinite prurigineuse, leave no doubt that they should come into question. In order to explain the gradual wandering of the symptoms from the conjunctiva to the chest in the single attacks and throughout life, a progressive increase in sensitiveness in the lower tracts and a progressive fatigue to irritation in the upper tracts must be assumed. Such an assumption is not overrash, since it may be seen analogously in physiology by the development of different nerve tracts at different periods of life, in pathology by the systematic transference of the predisposition to disease from one part of an organ to another.

Old writers insisted on the similarity of whooping-cough and asthma, as well as of paroxysms of sneezing with epilepsy. "Epilepsiæ sternutationem finitimam esse," says Theophilus Bonetus. Nor does any one doubt to-day that every epileptic and epileptoid explosion presupposes a special, more or less abnormal condition of tracts affected by the irritation. If, now, we allow the word neurosis for this abnormality which we cannot demonstrate, we may, with Ferber, call hay-fever "a neurosis of the vagus allied to whooping-cough," provided we add and also of the trigeminus, which contains the sensory tracts from the conjunctiva, nose, and pharynx. On account of the temporary deterioration of certain nerve tracts it would not be unreasonable to describe the disease, with Beard, as a partial neurasthenia, or as having a partial resemblance to neurasthenia. By these names as much is conveyed as by the expressions rhinobronchitis spasmodique (Guéneau de Mussy), periodic hyperesthetic rhinitis (J. Bloom), coryza vasomotoria periodica (John N. Mackenzie), etc.

We transfer, therefore, the irritability ("reizbare Schwäche") existing during the attack of Bostock's catarrh in certain organs to their sensory nerve tracts. To go further, and designate the exact place in the nerve affected by this loss of normal tone,—for instance, to assume with John Mackenzie a functional disturbance of the secretory center for the nose, etc., of the sphenopalatine ganglion, and of the cervical

sympathetic, or to assert with Sajous an inflammatory affection of the sphenopalatine ganglion as a cause for the special irritability of the mucous membrane under it,—would be to insist on the determination of undisputed facts.

The question whether the cause of this irritability is endogenous or exogenous throws the pathogenesis of the disease entirely into the region of hypothesis. One of the most interesting and, on first sight, satisfying, hypotheses was suggested by Kinnear in order to demonstrate the endogenous origin of the disease. At the basis of the gouty constitution, he affirms, there arises under the first action of the sun's heat a hyperemic condition of the nerve-centers of the fifth, seventh, ninth, and tenth pairs of nerves, and then any external irritation, let it be of a mechanical or other nature, is sufficient to call forth the symptoms of the disease, which at the same time continues subject to the irritation.

It is evident that Phöbus's abstract experimental principle, which affirms the scent of grasses and the pollen to be injuriously effective only during the summer heat, would agree with this hypothesis perfectly, and the hay or pollen theory would, therefore, in association with this, supply a sufficient explanation of the whole disease, if there were not patients who were attacked by their catarrh before the summer heat, suffer from it without being sensitive to pollen, and continue in it after the pollen has passed away.

So we are eventually forced to the consideration of the only hypothesis remaining of all those that have been suggested—namely, that of Hemlholtz, that Bostock's catarrh is an infectious disease. This hypothesis readily explains the symptomatology, even without the assumption of a particular constitution of the nervous system, if the analogies of wound-tetanus, rheumatic chorea, and the spasmodic stage of whooping-cough are kept in view.

The striking dependence of the disease on season, and the alteration of the critical period in different countries, harmonize with the experience that the vitality of many lower forms of life is associated with different seasons of the year, which may change with the climate. The crawling out of the May-beetle, the June-beetle, the glow-worm, at their definite seasons; the corresponding picture of the one-day's fly (ephemeris) in certain months; the autumnal disease of the house-fly (caused by the Empusa muscæ); the relation between the blight of the barberry and the blight of corn, need only be mentioned to demonstrate the possibility of an annual disease recurring regularly due to low life-forms. Moreover, the typical course of the year's attack,

with its prodromal stage, corresponds to the behavior of an infectious disease. Further, the behavior of the symptoms in Bostock's catarrh has its analogy in other parasitic diseases; for instance, neuralgia of the fifth nerve in malaria, the spasmodic stage of whooping-cough, and the daily exacerbations of hay-fever differ only in the location of the disease in different nerve regions. The parasitic theory for malaria suggested by Binz on scientific grounds almost thirty years ago has finally become a scientific fact; the amœba of whooping-cough, sought diligently by Binz since that time, will not remain concealed much longer provided it is sought where it is to be found, and where it has been discovered in an analogous disease, rabies, in the nervous system; and, lastly, the conviction of Binz that Bostock's catarrh is a parasitic disease in Helmholtz's sense will eventually redound to his fame.

If it should be found that the excitant of the annual catarrh thrives as miasm on meadows and in hay, the popular designation hay-fever will be justified in the same sense as the name swamp-fever is justified for malaria.

Möbius says: "Der welcher klinische Einheiten schafft, ist zugleich auch ätiologisch thätig. Die Ueber-einstimmung der Krankheitsbilder, die klinische Einheit ist das Organon, mittelst dessen wir unseren Weg finden, auch ehe die Ursache wirklich erkannt ist." ("Clinical unity demands an etiologic unit. The harmony in symptomatology, that is, the clinical unity, is the Organon, by means of which we find our way even before the cause is actually known.") The unity of the picture described by Bostock requires a unique etiology. And only the combination of a living specific excitant with a particular predisposition can satisfactorily explain the pathogenesis. The cause of the entire disease is the peculiar local and general predisposition; the cause of the individual annual attacks is a living excitant. The cause of the daily exacerbations are the numerous external irritants toward which different patients manifest different degrees of sensitiveness, and among these pollen takes the first rank.

TREATMENT OF HAY-FEVER.

NOT one single case of Bostock's catarrh has so far been cured. On this even the writers most at variance with one another are agreed as long as they hold fast to the true conception of summer catarrh. Neither Bostock nor Phöbus, neither Blackley nor Morell Mackenzie, knew of a case which, after the most careful and most varied dietetic and medical or surgical treatment, could face with impunity the influences under which the disease annually recurred, and under which it suffered exacerbations.

But it is conceivable that these very indications pointed out by the predisposing causes of the disease were not carried out with sufficient thoroughness to procure protection against the unknown external agents; for these indications are clear, and should be followed out, even though their results cannot be logically demonstrated.

Prophylaxis should begin in children of predisposed races and susceptible families with the first years of life. Clothing suitable to the climate and not conducive to effeminacy, cold shower-baths and baths in order to tone up the nervous system, abstinence from rich albuminous and irritative foods and luxuries in order to ward off the arthritic constitution or uric acid diathesis, are measures that appear most important for the preservation of health so far as our knowledge of the prophylaxis of the disease extends. Moreover, these measures have been approved by patients who experienced their beneficial effects, even in cases of the outspoken disease.

It is necessary, too, to give early consideration to the protection of susceptible individuals from the external exciting and aggravating causes. For this we must insist on the shunning of the country at the critical period, the eschewing of blooming fields and hay-harvestings, and the avoidance of the heat of the early summer and of the direct rays of the sun.

When the disease once breaks out, and the first attack or a series of annual attacks has begun the long chain of yearly recurrences, these dietetic measures must be determinedly undertaken and carried out with patience. Since the disease shows a tendency to aggravation at every recurrence during the first half of the patient's life, the prevention of the next yearly attacks and of the exacerbations is the primary indication. For we know from other analogous diseases of the ner-

vous system that the susceptibility increases with every recurrence, and it is especially true in Bostock's catarrh that the occasional causes produce not only sudden, but even lasting harm.

The avoidance of the unknown and known causes associated with the dwelling-place of the patient not seldom meets with success, in that the patient escapes that particular yearly attack, or is affected less severely by it. The surest protection seems to be a sea voyage, provided it is begun before the critical period; though Walshe, Abbott Smith, and others report the continuance of the attack on the open sea in individual cases, in fact, they have seen it even developing at sea. A case reported by Hack suffered from an attack for a week on the voyage from Java. The "immune climates" which we enumerated before are found effective by the majority of patients. Wyman assures us of the immediate cessation of an already developed attack by a visit to the White Mountains, Adirondacks, Catskills, and certain parts of the Alleghanys; yet exceptions are to be found even here. A sojourn on the seacoast helps some, a trip to Italy, Spain, or the Orient helps others, to pass their critical time untormented. Yet Percival Hunt relates the case of a man aged forty-three, who traveled the world over for thirty-six years, sojourned in the West Indies, India, and Egypt, and yet succumbed every May, June, and July to his catarrh. Many recommend residence in a large city to avoid the annual attacks. Dr. Simpson, for instance, moved from the country to London, and remained well as long as he avoided parks and gardens; yet only for a few years, and then the benefit of the city ceased. Many since Bostock's time have reported that the cool moist air of a shady room would ameliorate the course of an attack even more than the keeping to such an artificial climate during the critical period would prevent the attack. I personally have seen a woman who, after a long series of bath cures, an extended gyneoclogic treatment, etc., experienced not only aggravation of her mistaken disease, but was finally brought to a condition of poverty that prevented her following out further treatment. I have seen her after many years go through her first endurable summer, and after that show increasing amelioration of the annual attack, due to the advice to avail herself of such a room climate.

Not a few patients who are afflicted with only mild attacks defy their malady in any place or situation, and seek to prevent its increase by the regular employment of cold shower or plunge baths, and even to keep themselves capable of a certain amount of light work. That not every one finds cold water beneficial is evidenced by Ferber's personal experience. He derived marked benefit by changing his ordi-

nary heavy for light clothing, by airing his sleeping-room at night through a neighboring compartment, and by giving up smoking.   W. S. Paget, himself a patient, warns us also against too heavy clothing, especially flannel.   At the same time, however, as might have been foreseen, the directly opposite was recommended as a cure.   The American, Rumboldt, assures us of full protection from the attack by his "special hygiene," into which the following enter as the most important requirements: Three suits of underwear, two pairs of stockings, lined hoods day and night, the allowing of the hair to grow till it covers the neck; in case of bald head, a wig; the washing with vaselin alone, and drying with a woolen towel, and under no circumstances must the patient get into a temper!

With equal seriousness Blackley advises those who cannot leave the country, and so escape the pollen, to close up the nostrils with pledgets of gauze 'wound around a wooden frame.   With the same view, O'Connell contented himself with vaselin tampons, but it was necessary to introduce them with special metal forceps some weeks before the hay-fever season (Beschorner).   Thorowgood rejected both respirators and obturators.   While W. S. Paget, Genth, and others, tried with closely fitting goggles of blue or dark gray glass to prevent the entrance of pollen into the eyes, and to prevent the irritative effect of bright light, Hannay proposed to close the lacrimal canal with small glass rods.   Besides the carrying-out of such sometimes reasonable, again nonsensical, hygiene, different drugs have been recommended. Of these, the nervines hold the first place.   Quinin, iron, and arsenic have been considered capable of lessening the attack by continuous prophylactic employment.   Rowe, Perey, Gordon, and Phöbus give quinin in small doses of 2 to 3 gr. (0.1 to 0.2 gm.) daily.   Combinations of quinin and iron, and of iron and arsenic, are given in most varying mixtures by other authorities.   For the same indications, others recommend nux vomica, asafetida, zinc oxid or valerianate, zinc phosphate, or brucia phosphate.   Not a few advise the continuous employment of certain narcotics and sedatives before and during the annual attack.   Opium, belladonna, atropin, aconite, hyoscyamus, preparations of bromid, and camphor have been again and again prescribed. That phenazone (antipyrin), phenacetin, salol, etc., should be administered might have been assumed; that they should prove even as little useful as many of the foregoing might have been almost predicted; for an acute, rapid cure—such as the majority of physicians who prescribe these medicines await with impatience, and expect from every new drug with naïve confidence—is to be attained in hay-fever just as

little as in many other diseases, and only a few comprehend and endeavor to produce the slow, methodic influencing of the patient.

But that effectual results may be obtained by methodic medication is seen from the reports both of those who recommend quinin, and others, especially Déchambre, who advised, with Trousseau, the quinin-belladonna cure. To follow Trousseau's treatment, a patient must take every five or six days, while fasting, 8 gm. of powdered cinchona bark in a cup of black coffee; on the other days pills containing 1 centigram of extract and 1 centigram of powdered root of belladonna, one pill on the first and second day, two on the third and fourth, and so on till the daily number reaches four or five pills. This last dose must be continued for fourteen days, and then gradually lessened in a reverse way. The cure, which lasts, therefore, about a month, must be repeated at due intervals. The first time after its employment a marked amelioration of the annual attack was experienced; since the attack failed to occur in the second year, the uncertain action of belladonna was replaced by the positive one of atropin, and then the result was complete (Déchambre).

With a similar purpose as Trousseau prescribed belladonna, so Morell Mackenzie prescribes for his patients, before the critical time, asafetida; 0.1 gm. of the compound asafetida pill-mass of the British Pharmacopœia (it contains two parts asafetida, 2 galbanum, 2 myrrh, 1 syrup) in combination with 0.06 gm. zinc valerianate in a pill, and orders this two to four times daily for weeks.

Tyrrell and Bishop endeavored to change the diathesis or expel the uric acid from the blood (therefore introducing another sort of prophylactic therapy) with salicylate of sodium, or a combination of this with phosphate of sodium. As an alternative, Bishop also tried sulphuric or citric acid.

Helmholtz believed he employed a specific treatment which killed or paralyzed the hypothetic excitant of hay-fever when, influenced by Binz's discovery of the germicidal action of quinin, he poured a concentrated watery solution of quinin sulphate (1 : 800) into the nose and paralyzed the amœba seen by him in the nasal mucus. Not a few following Helmholtz insisted on the beneficial effect of the local use of quinin, particularly Binz, Frickhöffer, Busch, Hurry, Wyman, Patton; but with the search after " more effective " means, and under the influence of the pollen theory, it was forgotten and fell into disuse. The irritative action of quinin on the nasal mucous membrane caused Patton to employ in one case—and not without benefit—the milder acting salicylic acid. Other followers of the microbic theory tried

other antiseptics, as Fergus, who used sulphurous acid per os and per nares (aqua sulfurosa to 20 drops every three hours and the inhalation of slowly burning flowers of sulphur in a mixture of two parts with one part of pulverized wood-charcoal).

To keep off and remove the irritating pollen, Elliotson recommended, as far back as 1831, the washing of the face and the rinsing of the nose with a solution of common salt. After him, hundreds of other things were tried in order to displace the pollen or blunt the nasal mucous membrane to its action and to that of other irritants.

Sprayings, paintings, pencillings, insufflations, snuffs, smelling bottles, smelling sponges, tampons, offered themselves in succession. They may be employed with the most different antiseptics and narcotics, caustics and astringents, agents which act mechanically, and evacuants, singly or in combination, together or following one another, till the patient becomes convinced "that this everlasting pencilling or powdering is almost as disagreeable as the disease itself." Then there have been used salt water, glycerin, borax solution, sodium phosphate solution (1 : 500), carbolic acid solution (1 : 100), bichlorid of mercury solution (1 : 5000), hydriodic acid and peroxid of hydrogen, sulphurous acid and ammonium carbonate, chloroform, eucalyptol. Then the changes are rung on chromic acid (10 : 100), lactic acid (20 to 50 : 100), acetic acid, sulphate of zinc, chlorid of zinc, lunar caustics. Camphor has been applied, or menthol, laudanum, extract of cannabis indica, morphin hydrochlorid and sulphate, atropin sulphate, cocain hydrochlorid in solution or substance, as powder or stick. Bismuth subnitrate or carbonate, powdered capsicum, powdered ipecacuanha, and every other imaginable errhine and sternutatory has been requisitioned. Every suggested expedient, every drug, together with every form and dose and combination in which it may be employed, finds its defenders and opposers asserting their claims in an almost endless series of publications.

Daley and Hack made the indication for local treatment of the nose especially compulsory. The path must be closed to reflexes. There was success and failure under the most different methods. Superficial cauterization of the nasal mucous membrane with the incandescent wire supplanted the insufficient effect of the so-called chemical cautery, and this, in turn, gave way to the deeper cauterization with the thermocautery. J. O. Rowe cut away the anterior portion of the "swollen" turbinated bone; Koser broke off small pieces from the bone. Price Brown at first cauterized sensitive spots on his turbinated bones in vain, and later amputated a piece of his uvula because it

appeared to him to be the site of origin of the reflex disturbance, but likewise in vain.

To the complaint that all recommendations of a local treatment left one in the lurch, was added a warning against the misuse of their employment. Rethi, Semon, and Laurent raised a warning against the thermocautery after the number of mutilations of the nasal cavity had reached shockingly high figures. Stickler, Woodward, and Mattison cried out, "Beware of the free use of cocain in hay-fever!" when the cocain habit began to be associated, in Canada and other countries, with morphinism in cases of hay-fever.

In regard to the question, Shall the nose be locally treated in hay-fever? experience answers: The disease and its symptoms certainly do not indicate a destructive treatment of the nasal mucous membrane. Singeing, cauterization, etc., in cases which are pronounced and not merely imaginary anomalies of the mucous membrane, are allowable procedures, though not much can be promised from the operations. Moreover, that mild caustics which act superficially are to be preferred under all circumstances to the deeply destructive, scarproducing ones, is asserted by even the writers who advise the cure of hay-fever by cauterization of the visibly normal nasal mucous membrane. Molinié, for instance, recommends only a superficial etching with the thermocautery; Sajous, only the application of glacial acetic acid, which is neither strong in its action nor poisonous, while it serves for the one purpose of holding off by superficial necrosis external irritants from the sensitive nerve tracts.

Other methods of rational treatment sprang up in response to more harmless hypotheses than the reflex theory of hay-fever proved to be.

To counteract the hyperemia of the cord, Kinnear and Husted applied ice-bags to the spinal column. Hutchinson and Beard toned up the sympathetic by central galvanization.

Many patients went over to homeopathy. Six cases mentioned by Phöbus tried it in vain, and yet, he continues: "The imagination having such an influence over the nervous system, especially in these patients, they wait expectantly. But fatal enlightenment more and more cuts the ground from under all marvels." Blackley, himself a homeopath, recommended all manner of homeopathic doses, yet he considered the only hope for the patient to be in flight from pollen. Mental suggestion still remains to be tried. At least, literature as to its employment is wanting.

Symptomatic treatment during the attack is indispensable. The intense itching in the eyes and nose is appeased by rubbing, which,

though unsatisfactory, all patients affirm is better than the strongest cocain solution or camphor, or the inhalation of ammoniac and carbolic acid. The burning and tickling in the throat are relieved by swallowing movements and smacking with the tongue when peppermint lozenges and everything else fail. The stinging in the ears is diminished by pressure of the finger in the meatus, though camphor plugs prove unsuccessful. Ferber, of Hamburg, recently asserted that in him the entire attack was made milder by energetic rubbing of the ears, and the benefit "stood in direct proportion to the vigor of the rubbing." The American, Charles E. Page, makes merry over this foolishness. Mustard paper to the wrist, plunging of the hands or elbows in hot water, are recommended by many for the sneezing, though the majority advise perfect quiet and absolute rest.

The measures that ameliorate nervous asthma sometimes help in an asthma attack in this disease, but not always. Potassium iodid, niter paper, terpin hydrate, the extract of Euphorbia pilulifera, of Grindelia robusta, of Lobelia inflata, as well as the many secret preparations made from them, as "Himrod's cure," have been frequently recommended, and now and then employed with benefit. That morphin never failed in hay-asthma is asserted only by those who have never treated a hay-asthma, or even a nervous asthma. Physicians of experience have observed even marked aggravation due to the injection of morphin, especially in those cases where an expiratory dyspnea was associated with a difficulty in inspiration. It is certainly true that morphin shows its power in many cases; consequently the danger of the habit is not slight in the asthmatic stage of Bostock's disease.

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